If our planned business activities in China fall within a restricted category under the China Catalog for Guidance for Foreign Investment, we will need to operate in China through a variable interest entity ("VIE") structure.

The China Catalog for Guidance for Foreign Investment sets forth the industries and sectors that the Chinese government encourages and restricts with respect to foreign investment and participation. The Catalog for Guidance for Foreign Investment is subject to revision from time to time by the China Ministry of Commerce. While we currently do not believe the development and marketing of roxadustat falls within a restricted category under the Catalog for Guidance for Foreign Investment, if roxadustat does fall under such a restricted category, we will need to operate in China through a VIE structure. A VIE structure involves a wholly foreign-owned enterprise that would control and receive the economic benefits of a domestic Chinese company through various contractual relationships. Such a structure would subject us to a number of risks that may have an adverse effect on our business, including that the Chinese government may determine that such contractual arrangements do not comply with applicable regulations, Chinese tax authorities may require us to pay additional taxes, shareholders of our VIEs may have potential conflicts of interest with us, and we may lose the ability to use and enjoy assets held by our VIEs that are important to the operations of our business if such entities go bankrupt or become subject to dissolution or liquidation proceedings. VIE structures in China have come under increasing scrutiny from accounting firms and the SEC staff. If we do attempt to use a VIE structure and are unsuccessful in structuring it so as to qualify as a VIE, we would not be able to consolidate the financial statements of the VIE with our financial statements, which could have a material adverse effect on our operating results and financial condition.

FibroGen Beijing would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.

We plan to conduct all of our business in China through FibroGen China Anemia Holdings, Ltd. and FibroGen Beijing. We may rely on dividends and royalties paid by FibroGen Beijing for a portion of our cash needs, including the funds necessary to service any debt we may incur and to pay our operating expenses. The payment of dividends by FibroGen Beijing is subject to limitations. Regulations in China currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in China. FibroGen Beijing is not permitted to distribute any profits until losses from prior fiscal years have been recouped and in any event must maintain certain minimum capital requirements. FibroGen Beijing is also required to set aside at least 10.0% of its after-tax profit based on Chinese accounting standards each year to its statutory reserve fund until the cumulative amount of such reserves reaches 50.0% of its registered capital. Statutory reserves are not distributable as cash dividends. In addition, if FibroGen Beijing incurs debt on its own behalf in the future, the agreements governing such debt may restrict its ability to pay dividends or make other distributions to us. As of March 31, 2019, approximately \$6.6 million of our cash and cash equivalents is held in China.

Any capital contributions from us to FibroGen Beijing must be approved by the Ministry of Commerce in China, and failure to obtain such approval may materially and adversely affect the liquidity position of FibroGen Beijing.

The Ministry of Commerce in China or its local counterpart must approve the amount and use of any capital contributions from us to FibroGen Beijing, and there can be no assurance that we will be able to complete the necessary government registrations and obtain the necessary government approvals on a timely basis, or at all. If we fail to do so, we may not be able to contribute additional capital to fund our Chinese operations, and the liquidity and financial position of FibroGen Beijing may be materially and adversely affected.

We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.

If roxadustat is approved for sale in China, most of our product sales will occur in local Chinese currency and our operating results will be subject to volatility from currency exchange rate fluctuations. To date, we have not hedged against the risks associated with fluctuations in exchange rates and, therefore, exchange rate fluctuations could have an adverse impact on our future operating results. Changes in value of the Renminbi against the U.S. dollar, Euro and other currencies is affected by, among other things, changes in China's political and economic conditions. Currently, the Renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. Any significant currency exchange rate fluctuations may have a material adverse effect on our business and financial condition.

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In addition, the Chinese government imposes controls on the convertibility of the Renminbi into foreign currencies and the remittance of foreign currency out of China for certain transactions. Shortages in the availability of foreign currency may restrict the ability of FibroGen Beijing to remit sufficient foreign currency to pay dividends or other payments to us, or otherwise satisfy their foreign currency-denominated obligations. Under existing Chinese foreign exchange regulations, payments of current account items, including profit distributions, interest payments and balance of trade, can be made in foreign currencies without prior approval from the State Administration of Foreign Exchange ("SAFE") by complying with certain procedural requirements. However, approval from SAFE or its local branch is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The Chinese government may also at its discretion restrict access in the future to foreign currencies for current account transactions. If the foreign exchange control system prevents us from obtaining sufficient foreign currency to satisfy our operational requirements, our liquidity and financial position may be materially and adversely affected.

Because FibroGen Beijing's funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen Beijing deposits its funds could adversely affect our business.

Banks and other financial institutions in China do not provide insurance for funds held on deposit. As a result, in the event of a bank failure, FibroGen Beijing may not have access to funds on deposit. Depending upon the amount of money FibroGen Beijing maintains in a bank that fails, its inability to have access to cash could materially impair its operations.

We may be subject to tax inefficiencies associated with our offshore corporate structure.

The tax regulations of the U.S. and other jurisdictions in which we operate are extremely complex and subject to change. New laws, new interpretations of existing laws, such as the Base Erosion Profit Shifting project initiated by the Organization for Economic Cooperation and Development, and any legislation proposed by the relevant taxing authorities, or limitations on our ability to structure our operations and intercompany transactions may lead to inefficient tax treatment of our revenue, profits, royalties, and distributions, if any are achieved.

In addition, we and our foreign subsidiaries have various intercompany transactions. We may not be able to obtain certain benefits under relevant tax treaties to avoid double taxation on certain transactions among our subsidiaries. If we are not able to avail ourselves to the tax treaties, we could be subject to additional taxes, which could adversely affect our financial condition and results of operations.

On December 22, 2017, the U.S. enacted the Tax Cuts and Jobs Act ("Tax Act") that instituted fundamental changes to the taxation of multinational corporations. The Tax Act includes changes to the taxation of foreign earnings by implementing a dividend exemption system, expansion of the current anti-deferral rules, a minimum tax on low-taxed foreign earnings and new measures to deter base erosion. The Tax Act also includes a permanent reduction in the corporate tax rate to 21%, repeal of the corporate alternative minimum tax, expensing of capital investment, and limitation of the deduction for interest expense. Furthermore, as part of the transition to the new tax system, a one-time transition tax is imposed on a U.S. shareholder's historical undistributed earnings of foreign affiliates. Although the Tax Act is generally effective January 1, 2018, GAAP requires recognition of the tax effects of new legislation during the reporting period that includes the enactment date, which was December 22, 2017.

As a result of the impacts of the Tax Act, the SEC provided guidance that allows us to record provisional amounts for those impacts, with the requirement that the accounting be completed in a period not to exceed one year from the date of enactment. As of December 31, 2018, we completed our analysis of the accounting for the tax effects of the Tax Act and no material adjustments were recognized as of December 31, 2018. The primary impact of the Tax Act relates to the re-measurement of deferred tax assets and liabilities resulting from the change in the corporate tax rate ("Corporate Tax Rate Change"), which was recorded as of December 2017. Developing interpretations of the provisions of the Tax Act, changes to U.S. Treasury regulations, administrative interpretations, or court decisions interpreting the Tax Act in the future periods may require further adjustments to our analysis.

Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.

We seek to protect the products and technology that we consider important to our business by pursuing patent applications in China and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. We note that the filing of a patent application does not mean that we will be granted a patent, or that any patent eventually granted will be as broad as requested in the patent application or will be sufficient to protect our technology. There are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications not to be granted, including known or unknown prior art, deficiencies in the patent application, or lack of originality of the technology. Furthermore, the terms of our patents are limited. The patents we hold and the patents that may be granted from our currently pending patent applications have, absent any patent term adjustment or extension, a twenty-year protection period starting from the date of application.

Intellectual property rights and confidentiality protections in China may not be as effective as those in the U.S. or other countries for many reasons, including lack of procedural rules for discovery and evidence, low damage awards, and lack of judicial independence. Implementation and enforcement of China intellectual property laws have historically been deficient and ineffective and may be hampered by corruption and local protectionism. Policing unauthorized use of proprietary technology is difficult and expensive, and we may need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability and validity of our proprietary rights or those of others. The experience and capabilities of China courts in handling intellectual property litigation varies and outcomes are unpredictable. An adverse determination in any such litigation could materially impair our intellectual property rights and may harm our business.

We are subject to laws and regulations governing corruption, which will require us to develop, maintain, and implement costly compliance programs.

We must comply with a wide range of laws and regulations to prevent corruption, bribery, and other unethical business practices, including the FCPA, anti-bribery and anti-corruption laws in other countries, particularly China. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

Anti-bribery laws prohibit us, our employees, and some of our agents or representatives from offering or providing any personal benefit to covered government officials to influence their performance of their duties or induce them to serve interests other than the missions of the public organizations in which they serve. Certain commercial bribery rules also prohibit offering or providing any personal benefit to employees and representatives of commercial companies to influence their performance of their duties or induce them to serve interests other than their employers. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with these anti-bribery laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the anti-bribery laws present particular challenges in the pharmaceutical industry because in many countries including China, hospitals are state-owned or operated by the government, and doctors and other hospital employees are considered foreign government officials. Furthermore, in certain countries (China in particular), hospitals and clinics are permitted to sell pharmaceuticals to their patients and are primary or significant distributors of pharmaceuticals. Certain payments to hospitals in connection with clinical studies, procurement of pharmaceuticals and other work have been deemed to be improper payments to government officials that have led to vigorous anti-bribery law enforcement actions and heavy fines in multiple jurisdictions, particularly in the U.S. and China.

It is not always possible to identify and deter violations, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

In the pharmaceutical industry, corrupt practices include, among others, acceptance of kickbacks, bribes or other illegal gains or benefits by the hospitals and medical practitioners from pharmaceutical manufacturers, distributors or their third party agents in connection with the prescription of certain pharmaceuticals. If our employees, affiliates, distributors or third party marketing firms violate these laws or otherwise engage in illegal practices with respect to their sales or marketing of our products or other activities involving our products, we could be required to pay damages or heavy fines by multiple jurisdictions where we operate, which could materially and adversely affect our financial condition and results of operations. The Chinese government has also sponsored anti-corruption campaigns from time to time, which could have a chilling effect on any future marketing efforts by us to new hospital customers. There have been recent occurrences in which certain hospitals have denied access to sales representatives from pharmaceutical companies because the hospitals wanted to avoid the perception of corruption. If this attitude becomes widespread among our potential customers, our ability to promote our products to hospitals may be adversely affected.

As we expand our operations in China and other jurisdictions internationally, we will need to increase the scope of our compliance programs to address the risks relating to the potential for violations of the FCPA and other anti-bribery and anti-corruption laws. Our compliance programs will need to include policies addressing not only the FCPA, but also the provisions of a variety of anti-bribery and anti-corruption laws in multiple foreign jurisdictions, including China, provisions relating to books and records that apply to us as a public company, and include effective training for our personnel throughout our organization. The creation and implementation of anti-corruption compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. Violation of the FCPA and other anti-corruption laws can result in significant administrative and criminal penalties for us and our employees, including substantial fines, suspension or debarment from government contracting, prison sentences, or even the death penalty in extremely serious cases in certain countries. The SEC also may suspend or bar us from trading securities on U.S. exchanges for violation of the FCPA's accounting provisions. Even if we are not ultimately punished by government authorities, the costs of investigation and review, distraction of our personnel, legal defense costs, and harm to our reputation could be substantial and could limit our profitability or our ability to develop or commercialize our product candidates. In addition, if any of our competitors are not subject to the FCPA, they may engage in practices that will lead to their receipt of preferential treatment from foreign hospitals and enable them to secure business from foreign hospitals in ways that are unavailable to us.

Uncertainties with respect to the China legal system could have a material adverse effect on us.

The legal system of China is a civil law system primarily based on written statutes. Unlike in a common law system, prior court decisions may be cited for reference but are not binding. Because the China legal system continues to rapidly evolve, the interpretations of many laws, regulations and rules are not always uniform and enforcement of these laws, regulations and rules involve uncertainties, which may limit legal protections available to us. Moreover, decision makers in the China judicial system have significant discretion in interpreting and implementing statutory and contractual terms, which may render it difficult for FibroGen Beijing to enforce the contracts it has entered into with our business partners, customers and suppliers. Different government departments may have different interpretations of certain laws and regulations, and licenses and permits issued or granted by one government authority may be revoked by a higher government authority at a later time. Navigating the uncertainty and change in the China legal system will require the devotion of significant resources and time, and there can be no assurance that our contractual and other rights will ultimately be enforced.

Changes in China's economic, political or social conditions or government policies could have a material adverse effect on our business and operations.*

Chinese society and the Chinese economy continue to undergo significant change. Changes in the political structure, regulations, and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy, but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the regulatory structure and structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes and structural changes, any of which could materially and adversely affect FibroGen Beijing's development and commercialization timelines, liquidity, access to capital, and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China. In addition, the changing government regulations and policies could result in delays and cost increases to our development, manufacturing, approval, and commercialization timelines in China.

Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may materially and adversely affect our business, financial condition and results of operations.

We are subject to China Labor Contract Law, which provides strong protections for employees and imposes many obligations on employers. The Labor Contract Law places certain restrictions on the circumstances under which employers may terminate labor contracts and require economic compensation to employees upon termination of employment, among other things. In addition, companies operating in China are generally required to contribute to labor union funds and the mandatory social insurance and housing funds. Any failure by us to comply with Chinese labor and social insurance laws may subject us to late fees, fines and penalties, or cause the suspension or termination of our ability to conduct business in China, any of which could have a material and adverse effect on business, results of operations and prospects.

Recent developments relating to the United Kingdom's referendum vote in favor of leaving the EU could adversely affect us.

The United Kingdom held a referendum on June 23, 2016 in which a majority voted for the United Kingdom's withdrawal from the EU, commonly referred to as "Brexit". As a result of this vote, negotiations are expected to commence to determine the terms of the United Kingdom's withdrawal from the EU as well as its relationship with the EU going forward, including the terms of trade between the United Kingdom and the EU. The effects of the United Kingdom's withdrawal from the EU, and the perceptions as to its impact, are expected to be far-reaching and may adversely affect business activity and economic conditions in Europe and globally and could continue to contribute to instability in global financial markets, including foreign exchange markets. The United Kingdom's withdrawal from the EU could also have the effect of disrupting the free movement of goods, services and people between the United Kingdom and the EU and could also lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which EU laws to replace or replicate, including laws that could impact our ability, or our collaborator's ability in the case of roxadustat, to obtain approval of our products or sell our products in the United Kingdom. However, the full effects of such withdrawal are uncertain and will depend on any agreements the United Kingdom may make to retain access to EU markets. Lastly, as a result of the United Kingdom's withdrawal from the EU, other European countries may seek to conduct referenda with respect to their continuing membership with the EU. Given these possibilities and others we may not anticipate, as well as the lack of comparable precedent, the full extent to which our business, results of operations and financial condition could be adversely affected by the United Kingdom's withdrawal from the EU is uncertain.

Risks Related to the Operation of Our Business

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, commercialization and administration capabilities or contract with third parties to provide these capabilities for us. As our operations expand and we continue to undertake the efforts and expense to operate as a public reporting company, we expect that we will need to increase the responsibilities on members of management in order to manage any future growth effectively. Our failure to accomplish any of these steps could prevent us from successfully implementing our strategy and maintaining the confidence of investors in our company.

If we fail to attract and keep senior management and key personnel, in particular our chief executive officer, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

We are highly dependent on our chief executive officer, Thomas B. Neff, and other members of our senior management team. The loss of the services of Mr. Neff or any of these other individuals would be expected to significantly negatively impact the development and commercialization of our product candidates, our existing collaborative relationships and our ability to successfully implement our business strategy.

Recruiting and retaining qualified commercial, development, scientific, clinical, and manufacturing personnel are and will continue to be critical to our success, particularly as we expand our commercialization operations. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

There is also significant competition, in particular in the San Francisco Bay Area, for the hiring of experienced and qualified personnel, which increases the importance of retention of our existing personnel. If we are unable to continue to attract and retain personnel with

the quality and experience applicable to our product candidates, our ability to pursue our strategy will be limited and our business and operations would be adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing, manufacturing and commercialization of our product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under state consumer protection acts. If we are unable to obtain insurance coverage at levels that are appropriate to maintain our business and operations, or if we are unable to successfully defend ourselves against product liability claims, we may incur substantial liabilities or otherwise cease operations. Product liability claims may result in:

- termination of further development of unapproved product candidates or significantly reduced demand for any approved products;
- material costs and expenses to defend the related litigation;
- a diversion of time and resources across the entire organization, including our executive management;
- product recalls, withdrawals or labeling restrictions;
- termination of our collaboration relationships or disputes with our collaboration partners; and
- reputational damage negatively impacting our other product candidates in development.

If we fail to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, we may not be able to continue to develop our product candidates. We maintain product liability insurance in a customary amount for the stage of development of our product candidates. Although we believe that we have sufficient coverage based on the advice of our third party advisors, there can be no assurance that such levels will be sufficient for our needs. Moreover, our insurance policies have various exclusions, and we may be in a dispute with our carrier as to the extent and nature of our coverage, including whether we are covered under the applicable product liability policy. If we are not able to ensure coverage or are required to pay substantial amounts to settle or otherwise contest the claims for product liability, our business and operations would be negatively affected.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, collaboration partners, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We upgraded our disaster and data recovery capabilities in June 2017, however, to the extent that any disruption or security breach, in particular with our partners' operations, results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and it could result in a material disruption and delay of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

We depend on sophisticated information technology systems to operate our business and a cyber-attack or other breach of these systems could have a material adverse effect on our business.

We rely on information technology systems to process, transmit and store electronic information in our day-to-day operations. The size and complexity of our information technology systems makes them vulnerable to a cyber-attack, malicious intrusion, breakdown, destruction, loss of data privacy or other significant disruption. While we have recently upgraded our disaster data recovery program, a successful attack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyber-attacks are becoming more sophisticated and frequent. We have invested in our systems and the protection and recoverability of our data to reduce the risk of an intrusion or interruption, and we monitor and test our systems on an ongoing basis for any current or potential threats. There can be no assurance that these measures and efforts will prevent future interruptions or breakdowns. If we fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to these systems, we could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows.

Our headquarters and data storage facilities are located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business, results of operations and financial condition.

We and some of the third party service providers on which we depend for various support functions, such as data storage, are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires.

We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, or otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place are unlikely to provide adequate protection in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above your purchase price.

In general, pharmaceutical, biotechnology and other life sciences company stocks have been highly volatile in the current market. The volatility of pharmaceutical, biotechnology and other life sciences company stocks is sometimes unrelated to the operating performance of particular companies and biotechnology and life science companies stocks often respond to trends and perceptions rather than financial performance. In particular, the market price of shares of our common stock could be subject to wide fluctuations in response to the following factors:

- results of clinical trials of our product candidates, including roxadustat and pamrevlumab;
- the timing of the release of results of and regulatory updates regarding our clinical trials;
- the level of expenses related to any of our product candidates or clinical development programs;
- results of clinical trials of our competitors' products;
- safety issues with respect to our product candidates or our competitors' products;
- regulatory actions with respect to our product candidates and any approved products or our competitors' products;
- fluctuations in our financial condition and operating results, which will be significantly affected by the manner in which we recognize revenue from the achievement of milestones under our collaboration agreements;
- adverse developments concerning our collaborations and our manufacturers;
- the termination of a collaboration or the inability to establish additional collaborations;
- the publication of research reports by securities analysts about us or our competitors or our industry or negative recommendations or withdrawal of research coverage by securities analysts;
- the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- the ineffectiveness of our internal controls;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market:

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- additions and departures of key personnel;
- announced strategic decisions by us or our competitors;
- changes in legislation or other regulatory developments affecting our product candidates or our industry;
- fluctuations in the valuation of the biotechnology industry and particular companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other stockholders;
- speculation in the press or investment community;
- announcement or expectation of additional financing efforts;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- changes in accounting principles;
- activities of the government of China, including those related to the pharmaceutical industry as well as industrial policy generally;
- performance of other U.S. publicly traded companies with significant operations in China;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters such as earthquakes and other calamities;
- changes in market conditions for biopharmaceutical stocks;
- changes in general market and economic conditions; and
- the other factors described in this "Risk Factors" section.

As a result of fluctuations caused by these and other factors, comparisons of our operating results across different periods may not be accurate indicators of our future performance. Any fluctuations that we report in the future may differ from the expectations of market analysts and investors, which could cause the price of our common stock to fluctuate significantly. Moreover, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

We have broad discretion in the use of the net proceeds from our underwritten public offerings of common stock completed on April 11, 2017 (the "April 2017 Offering") and August 24, 2017 (the "August 2017 Offering") and may not use them effectively.

The net proceeds from the April 2017 Offering is intended to be used to fund the expansion of product development in China, including developing roxadustat in additional indications beyond CKD, manufacturing and commercialization activities, as well as for general corporate purposes. The net proceeds from the August 2017 Offering is intended to be used to fund the expansion of product development, including our development of pamrevlumab beyond current Phase 2 programs, manufacturing and commercialization activities, as well as for general corporate purposes. These general corporate purposes, may include, among other things, funding research and development, clinical trials, vendor payables, potential regulatory submissions, hiring additional personnel and capital expenditures. However, we have no current commitments or obligations to use the net proceeds in the manner described above. Our management has broad discretion in the application of the balance of the net proceeds from the April 2017 Offering and the August 2017 Offering, and could spend the proceeds in ways our stockholders may not agree with or that fails to improve our business or enhance the value of our common stock. The failure by our management to use these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates.

If securities or industry analysts do not continue to publish research or reports about our business, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.*

As of April 30, 2019, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 39.40% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date and shares issuable upon settlement of restricted stock units that will vest within 60 days after such date. This percentage is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G, if any, filed with the SEC, which information may not be accurate as of April 30, 2019. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. The interests of this group may differ from those of other stockholders and they may vote their shares in a way that is contrary to the way other stockholders vote their shares. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

Additional remedial measures that may be imposed in the proceedings instituted by the SEC against five China based accounting firms, including the Chinese affiliate of our independent registered public accounting firm, could result in our consolidated financial statements being determined to not be in compliance with the requirements of the Exchange Act.

In late 2012, the SEC commenced administrative proceedings under Rule 102(e) of its Rules of Practice and also under the Sarbanes-Oxley Act of 2002 against the Chinese affiliates of the "big four" accounting firms, including PricewaterhouseCoopers Zhong Tian CPAs Limited, the Chinese affiliate of our independent registered public accounting firm. The Rule 102(e) proceedings initiated by the SEC relate to these firms' failure to produce documents, including audit work papers, in response to the request of the SEC pursuant to Section 106 of the Sarbanes-Oxley Act of 2002, as the auditors located in China are not in a position lawfully to produce documents directly to the SEC because of restrictions under Chinese law and specific directives issued by the China Securities Regulatory Commission ("CSRC"). The issues raised by the proceedings are not specific to our auditors or to us.

In January 2014, an administrative law judge reached an initial decision that the Chinese affiliates of the "big four" accounting firms should be barred from practicing before the SEC for a period of six months. In February 2015, the Chinese affiliates of the "big four" accounting firms each agreed to a censure and to pay a fine to the SEC to settle the dispute and avoid suspension of their ability to practice before the SEC and audit U.S.-listed companies. The settlement required the firms to follow detailed procedures and to seek to provide the SEC with access to Chinese firms' audit documents via the CSRC. If future document productions fail to meet specified criteria, the SEC retains authority to impose a variety of additional remedial measures on the firms depending on the nature of the failure.

We cannot predict if the SEC will further review the four firms' compliance with specified criteria or if such further review would result in the SEC imposing additional penalties such as suspensions or commencing any further administrative proceedings. Although it does not play a substantial role (as defined under PCAOB standards) in the audit of our consolidated financial statements, if PricewaterhouseCoopers Zhong Tian CPAs Limited were denied, temporarily, the ability to practice before the SEC, our ability to produce audited consolidated financial statements for our company could be affected and we could be determined not to be in compliance with the requirements of the Exchange Act. Such a determination could ultimately lead to the delisting of our shares from the Nasdaq Global Select Market or deregistration from the SEC, or both, which would substantially reduce or effectively terminate the trading of our stock.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our business, results of operations, financial condition and cash flows and future prospects.

While we currently have no specific plans to acquire any other businesses, we may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our present or future product candidates and business or otherwise offer opportunities for our company. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our existing stockholders' percentage of ownership;
- incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

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We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products or technologies, or employees or other assets of the acquisition target;
- · increases to our expenses;
- disclosed or undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- reprioritization of our development programs and even cessation of development and commercialization of our current product candidates;
- harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current directors or management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed prior to the end of their term only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- require a supermajority vote of the holders of our common stock or the majority vote of our board of directors to amend our bylaws; and
- require a supermajority vote of the holders of our common stock to amend the classification of our board of directors into three classes and to amend certain other provisions of our certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Moreover, because we are incorporated in Delaware, we are governed by certain anti-takeover provisions under Delaware law which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. We are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Changes in our tax provision or exposure to additional tax liabilities could adversely affect our earnings and financial condition.

As a multinational corporation, we are subject to income taxes in the U.S. and various foreign jurisdictions. Significant judgment is required in determining our global provision for income taxes and other tax liabilities. In the ordinary course of a global business, there are intercompany transactions and calculations where the ultimate tax determination is uncertain. Our income tax returns are subject to audits by tax authorities. Although we regularly assess the likelihood of adverse outcomes resulting from these examinations to determine our tax estimates, a final determination of tax audits or tax disputes could have an adverse effect on our results of operations and financial condition.

We are also subject to non-income taxes, such as payroll, sales, use, value-added, net worth, property, gross receipts, and goods and services taxes in the U.S., state and local, and various foreign jurisdictions. We are subject to audit and assessments by tax authorities with respect to these non-income taxes and may have exposure to additional non-income tax liabilities, which could have an adverse effect on our results of operations and financial condition.

On December 22, 2017, the U.S. enacted the Tax Act that instituted fundamental changes to the taxation of multinational corporations. The Tax Act includes changes to the taxation of foreign earnings by implementing a dividend exemption system, expansion of the current anti-deferral rules, a minimum tax on low-taxed foreign earnings and new measures to deter base erosion. The Tax Act also includes a permanent reduction in the corporate tax rate to 21%, repeal of the corporate alternative minimum tax, expensing of capital investment, and limitation of the deduction for interest expense. Furthermore, as part of the transition to the new tax system, a one-time transition tax is imposed on a U.S. shareholder's historical undistributed earnings of foreign affiliates. Although the Tax Act is generally effective January 1, 2018, GAAP requires recognition of the tax effects of new legislation during the reporting period that includes the enactment date, which was December 22, 2017.

As a result of the impact of the Tax Act, the SEC provided guidance that allows us to record provisional amounts for those affected items, with the requirement that the accounting be completed in a period not to exceed one year from the date of enactment. As of December 31, 2018, we completed our analysis of the accounting for the tax effects of the Tax Act and no material adjustments were recognized at year end. The primary impact of the Tax Act relates to the re-measurement of deferred tax assets and liabilities resulting from the Corporate Tax Rate Change, which was recorded as of December 31, 2017. Developing interpretations of the provisions of the Tax Act, changes to U.S. Treasury regulations, administrative interpretations or court decisions interpreting the Tax Act in the future periods may require further adjustments to our analysis.

Our amended and restated certificate of incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may

incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

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Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in our product candidates and maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS.

Use of Proceeds from Initial Public Offering of Common Stock

On November 13, 2014, our Registration Statement on Form S-1, as amended (Reg. Nos. 333-199069 and 333-200189) was declared effective in connection with the initial public offering of our common stock. There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on November 14, 2014.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES.

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

ITEM 5. OTHER INFORMATION.

None.

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ITEM 6. EXHIBITS.

Exhibit			Incorporation By Reference			
Number	Exhibit Description	Form	SEC File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation of FibroGen, Inc.	8-K	001-36740	3.1	11/21/2014	
3.2	Amended and Restated Bylaws of FibroGen, Inc.	S-1/A	333-199069	3.4	10/23/2014	
4.1	Form of Common Stock Certificate.	8-K	001-36740	4.1	11/21/2014	
4.2	Investor Rights Agreement by and among FibroGen, Inc. and certain of its stockholders, dated as of December 1995.	S-1	333-199069	4.2	10/01/2014	
4.3	Investor Rights Agreement by and among FibroGen, Inc. and certain of its warrant holders, dated as of February 8, 2000.	S-1	333-199069	4.7	10/01/2014	
4.4	Warrant to Purchase 11,076 Shares of Common Stock issued to Bristow Investments, L.P, dated as of February 8, 2000.	S-1	333-199069	4.12	10/01/2014	
4.5	Common Stock Purchase Agreement by and between FibroGen, Inc. and AstraZeneca AB, dated as of October 20, 2014.	S-1/A	333-199069	4.17	10/24/2014	
4.6	Shareholders' Agreement by and among FibroGen International (Cayman) Limited and certain of its shareholders, dated as of September 8, 2017.	10 - Q	001-36740	4.6	11/8/2017	
10.26(xxxvi)*†	Amendment No. 33 to the Process Development and Clinical Supply Agreement, by and between FibroGen, Inc. and Boehringer Ingelheim Biopharmaceuticals GmbH, effective as of January 4, 2019	_	_	_	_	
31.1*	Certification of Chief Executive Officer, as required by Rule 13a-14(a) or Rule 15d-14(a).	_	_	_	_	
31.2*	Certification of Chief Financial Officer, as required by Rule 13a-14(a) or Rule 15d-14(a).	_	_	_	_	
32.1*	Certification of Principal Executive Officer and Principal Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350)(1)).	_	_	_	_	
101*	Financial statements from the quarterly report on Form 10-Q of the Company for the quarter ended March 31, 2019, formatted in XBRL: (i) the Condensed Consolidated Balance Sheets, (ii) the Condensed Consolidated Statements of Operations (iii) the Condensed Consolidated Statement of Comprehensive Loss, (iv) the Condensed Consolidated Statements of Cash Flows and (v) the Notes to the Condensed Consolidated Financial Statements.	_	_	_	_	

^{*} Filed herewith

[†] Confidential treatment requested

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

FibroGen, Inc.

Dated: May 9, 2019

By: /s/ Thomas B. Neff

Thomas B. Neff

Chairman of the Board and Chief Executive Officer

(Principal Executive Officer)

Dated: May 9, 2019

By: /s/ Pat Cotroneo

Pat Cotroneo

Senior Vice President, Finance and Chief Financial Officer

(Principal Financial and Accounting Officer)

EXHIBIT M

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Wednesday, June 12, 2019 6:00 PM GMT

Call Participants	 3
Presentation	4
Question and Answer	

Call Participants

EXECUTIVES

Elias Kouchakji Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

K. Peony Yu *Chief Medical Officer*

Thomas B. Neff Founder, Chairman & CEO

ANALYSTS

Kyuwon Choi Goldman Sachs Group Inc., Research Division

Presentation

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay, we'll continue with the next session. Good morning, everyone. I'm Paul Choi, the U.S. mid-cap biotechnology analyst here at Goldman Sachs. And in the audience here, from the team, we have Corinne Jenkins. Our next session will be with FibroGen. And to my left, from the management team, we have Dr. Tom Neff, CEO, who will introduce the rest of the team here for you to the audience.

Thomas B. Neff

Founder, Chairman & CEO

Yes. Thank you, Paul. Dr. Peony Yu is on my immediate left, our Chief Medical Officer; and at the end, Dr. Elias Kouchakji, who is both Global Safety Head for the anemia program, roxadustat, and also the Head of Clinical Development for the pamrevlumab program. So that's the team for this morning.

Question and Answer

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. Thank you for that. So perhaps we'll kick off the Q&A and -- with perhaps an overview of the data and the top line results you and your collaborators recently presented. So either Tom or Peony to walk us -- perhaps can walk us through the data, understand what were the results in the respective populations and how to think perhaps, starting with that, just what were the results on top line and what we can expect in terms of a little more details as we proceed in the future.

Thomas B. Neff

Founder, Chairman & CEO

So Peony, please go ahead on this.

K. Peony Yu

Chief Medical Officer

Okay. Yes. So we've recently reported exciting positive full adjudicated cardiovascular safety results from the largest Phase III CKD anemia program. We believe we have compelling evidence confirming roxadustat's cardiovascular safety to support our regulatory filings. In Europe, the primary cardiovascular safety endpoint is MACE+, and in U.S., it is MACE. In dialysis, we compare roxa to EPO, and in nondialysis, the comparison is to placebo, which is the gold standard for safety comparison. We believe our MACE+ results have met the European criteria for cardiovascular safety in dialysis and in nondialysis. For U.S., we believe our MACE results in dialysis and in nondialysis also supports the conclusion of no increased cardiovascular safety risk.

To further frame the safety result, along with efficacy together, in dialysis, I also want to emphasize MACE + superiority in incident dialysis pool of over 1,500 patients. Lower MACE+ risk than EPO in incident dialysis may allow roxadustat to become first-line therapy for patients starting dialysis and continuing long-term anemia treatment. Superiority in transfusion avoiding EPO hyporesponsiveness are important benefits too in this population. For nondialysis, we believe safety noninferiority against placebo in MACE and MACE+ coupled with efficacy benefits like transfusion reduction, attenuation of renal progression, measuring eGFR change and improvement in quality of life when treating patients with roxa may give us the opportunity to improve and expand anemia care in the very large CKD nondialysis patient population.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. You've mentioned 2 different things with regard to the European side and the U.S. side. And maybe just starting with the European side, your -- it sounds like your level of comfort there and your partners is fairly high with respect to meeting the MACE criteria in both populations. And I just want to maybe clarify that with regard to the regulatory outlook in Europe. Is that what you and your collaborators are articulating with meeting the criteria in both populations?

K. Peony Yu

Chief Medical Officer

Yes. So we have -- this data has been shared with our partner Astellas, and jointly, we are very well prepared to submit MAA.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

And with respect to timing on the MAA, could you maybe just remind us or update us what you're thinking that you and your partners will have in terms of announcement with that timing, when we would potentially expect things like updates on the filings and so forth?

K. Peony Yu

Chief Medical Officer

Yes. So we are preparing common technical document that can be -- CDT, and that can be used for U.S. and Europe with slight modification. And so the target submission time line for MAA is around November just right after U.S. target time line, September-October time frame.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. Great. And then on the U.S. side, you also talked about your level of comfort there. And understanding, would the timing there be similar with regard to filing out potential applications here in the U.S.? And how are you thinking about those mechanics?

K. Peony Yu

Chief Medical Officer

Okay. So for the U.S., so our team has been conducting data analysis and preparing the documents needed for NDA. We have a pre-NDA meeting with the FDA at the end of July to discuss the full content of the NDA as well as details of some of the analysis, especially in nondialysis. And so we -- so this is part of the overall time line for our targeted submissions in the September-October time frame.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. With respect to getting a little more details on the top line results, can you maybe help us understand what would perhaps be a appropriate medical conference or forum where you might present the full data? And you and your colleagues -- or collaborators, excuse me, have you reached an agreement on when you would present the data and what exactly you would present?

K. Peony Yu

Chief Medical Officer

Yes. Well, you know that our top priority are the NDA and MAA submission. And in terms of medical conferences, we are planning to present Phase III results, this is in collaboration with our partners, and do this in nephrology conference and the first one that comes to mind is the ASN in November of this year. We are also making preparations of a full data disclosure manuscript, a high priority amongst our joint team in the 3 companies.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. So the American Society of Nephrology would potentially be the most logical forum for full details on -- would this be across all populations or just the...

Thomas B. Neff

Founder, Chairman & CEO

I think the manuscripts will be ultimately full details because there's just so much data to get to. These are huge studies. At ASN, we'll do our best to cover certain topics, but I think that we're expecting the manuscripts will be needed to get to everything.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Got you for that. Okay. You mentioned your timing expectations in terms of your pre-NDA would be roughly in the July time frame. Would you have, do you think, any subsequent discussions in the back half of this year prior to your NDA filing? And would that be something from a timing perspective that you would update investors on? Or how do you think about that, Tom?

Thomas B. Neff

Founder, Chairman & CEO

We're considering the possibility of that, yes. Depends on the timing. But if the timing goes according to plan, now we're looking at end of August time period to do something.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

And would that be with respect to both populations? Or would you -- do you think this would have to be bracketed out into 2 populations [indiscernible]?

Thomas B. Neff

Founder, Chairman & CEO

We'd like to be able to show a different angle of refraction on the data, so give a different cut of it, so investors can appreciate a little more some of the issues that they've been debating.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. Perhaps after you think about the submissions on the U.S. and European side, is there any thoughts on the potential for an adcom here? I guess that's a question that investors may have. And maybe how do you think about that possibility? What are your levels of preparation, I guess, in case that is an occurrence or an event that occurs, how do you think about that?

Thomas B. Neff

Founder, Chairman & CEO

Given the history in dialysis, some of the sorted history in dialysis, we expect there will be an adcom, and so we're planning accordingly. And we have very, very good data, so I think it would be really interesting to see how that goes.

K. Peony Yu

Chief Medical Officer

Plus, we have very strong support from KOLs in the nephrology field, and we have been working with these experts for a number of years. So we think that if adcom does come up, we will be well prepared. But at the same time, decision on adcom is based on FDA's decision after they review the complete NDA file.

Thomas B. Neff

Founder, Chairman & CEO

But it is the baseline planning assumption that there will be an adcom.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

The baseline case for you...

Thomas B. Neff

Founder, Chairman & CEO

That's right.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

And your collaborators will be for an adcom here?

Thomas B. Neff

Founder, Chairman & CEO

Yes.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. With that in mind, perhaps thinking about commercialization here and thinking about what the market development might look like, can you talk about your level of preparation and how you're thinking about commercialization? And maybe starting there and then we can dive into that a little deeper.

Thomas B. Neff

Founder, Chairman & CEO

Okay. So AstraZeneca is our collaborator in the U.S. and Astellas in Europe. These have been long-term relationships. I think that the recent datasets, in particular, after the adjudication on blind revealed opportunities, frankly, neither side, Europe or the U.S., was expecting. And so for instance, with Astellas in Europe, the idea that MACE+ would be superior in efficacy and safety to EPO is a big change in opportunity set from their perspective. And they are working hard to reprioritize and redefine investment, investments getting larger. I think without question, this program is very important to each of these companies in terms of their highest priority new programs. Each of them will name first 1 or 2 in their whole company and that continues. So I think that we see that aspect, if anything, expanding investment, heightening the energy level and so on.

With AstraZeneca in the U.S., which is a company that's the largest renal sales company now, they have a lot of capability. They are preparing appropriately. We help them with medical affairs as it relates to the large dialysis organizations. We also help them with commercial market preparation in other areas such as the CMS negotiations for new technology like this. So there's a lot of areas of contact and interaction between our company and AZ. But we are looking to them to provide the muscle on the ground, so to speak, in the U.S. So things are moving along and, I'd say, an appropriate level of excitement and response based on the data.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

As we think about the landscape with regard to reimbursement in the dialysis and nondialysis setting, there's obviously been some evolution over time with regard to the EPO. There was certainly more -- call it, a decade-plus ago, more flexibility with regard to pricing, but then the model evolved, as you know, to more a bundled arrangement. How do you think about the payers, both on the private and public side, thinking about bundling that exists currently in the market? And where do you see roxa perhaps fitting in here? And perhaps is there -- how does the model accommodate your product?

Thomas B. Neff

Founder, Chairman & CEO

Yes. So I think we disclosed a few years ago that CMS had indicated that depending on the results, and I think the results are now in, that they were allowed to look at roxa as new technology and as such had the freedom of flexibility to strike a different arrangement with us if they so chose to do. What I can say now is that they have a project team that's been working on roxa for several years, and there's a point of interaction on several different issues. Been going on for a while. So we'll see what happens. But I think that it's a little bit hard to predict right now what it will turn out to be in the dialysis setting. I don't expect any strict bundle or any strict definition by just oral therapy. I think it's going to be something else. Outside of that, Part D medicines in pre-dialysis settings are pretty well understood. So I don't think that's going to be such a big issue.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. Maybe on the market development side, with respect to the competitive landscape, there are various factors, such as biosimilars potentially launching in the U.S. on the EPO side at some point in the foreseeable future potentially. But in terms of other therapeutic modalities, are there anything -- is there

anything out there that keeps you awake at night in terms of a competitive perspective outside of the EPO or biosimilars that you see coming on here that are on your radar screen with respect to competitive pressures?

Thomas B. Neff

Founder, Chairman & CEO

Well, we're in a place now where we have safety data and efficacy data that's superior to EPO in a U.S. setting. So I think that situation and all the implications around it is being reevaluated a bit. I think we'll be watching with some interest whether any of the HIF companies can get enough momentum to sort of they'll -- fast follower-type companies. But as it relates to ESAs or PEG-ESAs, I'm not so sure we're thinking that's a major competitive risk at this point.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

So you think primarily of the HIF, whether it's 2 alphas or other things like that, being relatively early stage in terms of the competitive landscape and not differentiated...

Thomas B. Neff

Founder, Chairman & CEO

Well, speaking more broadly, in China, we -- for instance, we have a very large operation, and we don't see HIF competition in the next 3 to 5 years. In Japan, we do see competition because there are other companies lining up for launch, and that's probably a reflection of the different regulatory environments in each of those countries, what's possible. In the U.S., there are a couple of factors related to how we've differentiated ourself and I think in one respect doing the work to do placebo study in CKD and show that we are as safe as the placebo control arm is a very exciting place to be for purposes of trying to build a marketplace. That took a lot of effort over a long period of time. And I know that FDA has expressed in various ways that they're very pleased with the progress over the years and what's gone on.

And in the dialysis setting, we also set out a thesis, 2012, 2013, that an incident dialysis comparison would be favorable to the roxa technology over EPO. And so we've ended up creating a pool of almost 1,600 patients in a incident dialysis setting where from the time a patient might initiate dialysis any time in the next 4 months they randomize to either roxa or EPO, then we study them all the way through and we've had outstanding results in this area. We think it's the most fair comparison of EPO to roxa. We think it opens the door to roxa being recommended as a first medicine, both in the U.S. and in China. And so I think that we'll see how it develops. You can never be sure until you get there, but it looks very, very promising at this point.

And so I think when I look at the competitor HIF companies, they did not invest in these kinds of studies in -- on nondialysis, they're doing comparisons to ESA. That is really a market that has been deemphasized really at FDA's direction for a long period of time now.

And then in the dialysis setting, I think the largest incident population that we're aware of amongst the other companies doing HIF is about 350 patients, and that's not nearly big enough to deal with the powering of statistical results we're trying to get to. So we are very hopeful that we have a strong competitive position in the U.S., and we think probably in Europe, we're going to see very similar dynamics develop, although Europe is a much more complicated picture in terms of cross-licensing stuff than the U.S. So we'll just have to wait and see how it develops in Europe, I think.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. Maybe returning to the regulatory landscape for a moment. As investors do have access and awareness of what the product looks like in the China market currently, you have sort of a label that's a product approval that gives investors a way to assess what kind of claims and data and so forth are available overseas. But as you think about the U.S. side, if you were to think about what is perhaps a base case based on the data you've seen so far to think about your label, potential claims and what data

might be included, how would you perhaps frame a base case for us? And what would sort of be the most optimistic case in terms of what a U.S. FDA-approved label might look like, would you say?

Thomas B. Neff

Founder, Chairman & CEO

So Peony, I'm probably going to let you to try to answer this, but I'm going to start with one observation, and that is, in China, we've actually earned a label where the treatment range is 10.5 to 12 hemoglobin. And so in China, ESA is limited to 11. And so the regulators were very comfortable in giving that difference initially with roxa based on the data. We don't know if something like that is possible in the U.S., and we are not gunning for it as a primary goal. It's just -- it was inappropriate given the circumstances a few years ago to be thinking about it that way. But it is an issue that we're seeing develop in a favorable manner elsewhere. So with that, Peony, please go ahead on...

K. Peony Yu

Chief Medical Officer

Thank you, Tom. So Tom mentioned the target hemoglobin range in the China label. Another very important differentiation in the China label that sets roxa apart from ESA is the product warning precaution. And the EPO label in China has warning of death, MI, stroke and tumor. And those terms do not appear as warning on our roxa label in China. And that is because the Chinese regulators recognize roxadustat as a different class of drug from ESA and label according to what the data showed. Now we are -- we know that our FDA has a lot of excellent clinical scientists, and we are hopeful that given the data we generated and showing cardiovascular safety comparing to placebo and superiority in MACE+ against EPO, that our FDA will also label our drug according to what the data they would be reviewing.

Thomas B. Neff

Founder, Chairman & CEO

I think a key goal in the U.S. was -- with CKD population, a placebo study was to show noninferior to placebo, to show that there isn't any incremental risk of measure so that it opens the door to the logic it shouldn't have a black box for placebo. Therefore, roxa should not have black box and go from there in dealing with dialysis. And it's turned out as we hoped for. So I think this will be very interesting. Yes.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

With respect to the 2 different populations that will be reviewed, perhaps as you think about the market over time and thinking about what patient duration could look like as it evolves and you get more market information, can you maybe, first of all, remind us how long -- what is the longest or, on average, patients have been treated here across the various studies? And then how do you think about that perhaps evolving in a real-world setting as you commercialize in the U.S.?

K. Peony Yu

Chief Medical Officer

Yes. Paul, great question. Roxadustat exposed patient, the longest time is more than 6 years in our extension from our Phase II. And we have a small number of patients who just refused to get off this drug because they love it. And in our Phase III studies, we have substantial number of patients with over 2 years of exposure. And in fact, that's around the average amount of time on study. And what we have found is the drug is very durable. And what I mean by that is that the dose required to maintain that hemoglobin seems quite stable over time. And I think that one of the big reasons is that our drug mobilizes iron and is not affected by inflammation, which both of those are issues with EPO.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. In the time remaining, perhaps I want to switch a little bit -- switch gears here and maybe switch to the pamrevlumab program and think about that and maybe we can just start with regard to a quick

overview of the various development programs and where they are, maybe starting with that, to kick it off.

Thomas B. Neff

Founder, Chairman & CEO

Dr. Kouchakji is going to address these questions. Elias, please go ahead.

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Thank you, Tom. Thank you, Paul. Recently, we are starting, as we said, 2 Phase III studies. The first one is IPF, idiopathic pulmonary fibrosis, and the second one is in pancreatic cancer, specifically locally advanced and resectable pancreatic cancer. These are 2 very important programs. I would like to emphasize that the FDA granted an orphan designation for all 3 indications, including the Duchenne muscular dystrophy, and we received Fast Track designation for pamrevlumab for IPF in locally advanced pancreatic cancer. But most importantly now is there is big interest in our study in Duchenne muscular dystrophy. Specifically, we are conducting in nonambulatory patients.

The data so far that we have announced that the 21 patients who are enrolled in this study, open label, completed 1 year of therapy in the mid of March. We started doing administrative analysis of this data. We are doing this analysis in multiple parameters: pulmonary functions; cardiac functions; muscle functions; and imaging, MRIs. And we have seen a positive results in all these parameters. And I think this is another unique aspect of this drug and for this development of pamrevlumab.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. Maybe starting with the IPF program, there are some approved therapies on the market, such as Esbriet from Roche, Intermune and so forth, that have been, I think, quite surprising in terms of the market and become, in many respects, the standard of care for a segment of the population, but there are also some trade-offs with regard to adverse events and so forth. So can you maybe frame for us what percentage of patients are appropriate for Esbriet? And is that a benchmark you think about from a competitive perspective? Or are there patient populations where you think a need is not being met currently by some of the approved therapies?

Elias Kouchakii

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

So there is very clear an unmet need for a patient population who are either being treated and did not respond or treated and could not tolerate. And additionally, there is a patient population who has declined totally the treatment due to the fact that they're concerned over the safety of these 2 molecules. As you know that for pirfenidone, the skin toxicity, that this can prevent a lot of people from performing their daily activities. And then liver toxicity could not be dismissed in nintedanib. This population, if it is left out, as there is nothing else they can get into and this population required it, and I think this is the population at this time we are addressing.

And we think pamrevlumab, if the Phase III study is successful, could be at the same time the first-line therapy for all patients before any other patients. So that's why we are emphasizing to enroll our patients, the patients who are currently not on treatment. This, at the same time, could be an ethical thing because just trying to re-treat the patient who is treated is not sufficient, as we are leaving a big section of the population that's never been addressed.

Kvuwon Choi

Goldman Sachs Group Inc., Research Division

Great. And maybe just in terms of the patient sizing. What percentage of the population do you think that would describe roughly, Elias?

Elias Kouchakii

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

I think at this time, our assessment, this population is between 40% to 50% of the population.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

In IPF?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

In IPF. Yes. And I would just emphasize the IPF diagnosis is improving especially with the new diagnosis, that is, guidelines which were put in 2018 in ERS by Raghu and that is going to increase the number of subjects who is going to be diagnosed with IPF.

Thomas B. Neff

Founder, Chairman & CEO

One of our briefing partners for FDA, Dr. Luca Richeldi, went through all these populations, and FDA reviewers were really surprised how much the 2 approved therapies had fallen into disuse for various reasons. And that's a key aspect of why we're allowed to go ahead.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Maybe just to frame -- help investors understand and frame expectations, can you maybe just review for us what the prior clinical data has shown? And how do you think about that translating into your larger Phase III population?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

I think it's very important to share that -- to remind everyone, first of all, from the FVC decline, we showed a much bigger -- a slower decline in FVC versus placebo compared to other 2 products. I'm not going to say instead we are a direct comparison, but at the same time, our study is against placebo and has reached a statistical significance in Phase II studies, which is not really required. And that one of the biggest aspect. There is another aspect as is we take a look at the patient who declined, and a patient decline is considered, you had a patient decline more than 10% in FVC percent predicted or died on the studies. If you take a look at that difference between these 2 study arms, there is proportionally 60% more decline in the placebo for this. And if you take a look at the other 2 products, they have not shown that big margin in differentiation in the severe decline.

The third part, which again is unique to pamrevlumab, is our QHR CT, the quantitative high-resolution CT scans measuring the fibrosis. And this we've shown time and time again, we did it in 049 study and similarly in 067 study that we've shown that the fibrosis in some patients, at least 1/3 of these patients have stabilization or decrease in the total volume of the fibrosis, that is, in either any of these 2 molecules have shown that they can capable to do.

Thomas B. Neff

Founder, Chairman & CEO

There are no other positive results with HR CT besides the ones that we have. Yes.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Maybe shifting gears, in the time left we have, to the pancreatic side. This historically, obviously, has been a very, very tough solid tumor to treat. And can you maybe -- what is the case for optimism here for making the investment? What have you seen so far that supports do you think proceeding here just given that the historical success rate obviously has been very, very low here in this area?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

It's hard to say that, as I mentioned, that this is especially -- we are going after a special population, a subpopulation, which is very hard to treat. Usually, these patients have best outcome if they can be going to surgery. There is a limitation of involvement of the tumors around the vessels that's prevented them from being resectable. The uniqueness of our Phase II study is that we increase the resection in this population to 33%. But if we take a look into the resectability, that is another big assessment, that is, the patient can go to the surgeon and assess for the resection. So that has increased to 75%.

So we think we have a very unique proposition here that we can change the positioning of the tumors and make the tumors more selective for resection. And that is exciting at the same time due to the fact that FDA stated that if our Phase III study showed a resection rate favorable of pamrevlumab assays will be sufficient for it to be considered a surrogate endpoint for accelerated approval, this is exciting for someone like me who is a surgeon by training, which is a transplant surgeon. We do resect pancreatic cancer. And that is a very important part, that is, we are looking for something that can help us bring this patient assays. At the same time, went and said very clearly, patient resected, and resection has a link to increase of time of survival. That is very well documented, and that is what we are looking for.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. So I don't know how you keep track of all these programs, but you're also working on DMD as well. And I guess, my question here is that the landscape in DMD has been one of the biggest focal points in biotech for the past couple of years, and you are also seeing gene therapy approaches being developed. And so how do you think about, I guess, that perhaps potentially affecting the market opportunity in the nonambulatory population, if there is some sort of clinical success? Does that change your opportunity in terms of your addressable patient pool? And -- or do you think -- how do you think about that perhaps?

Thomas B. Neff

Founder, Chairman & CEO

So yes, all the things you said are true. We started way before the recent antisense-type genetic targeted molecules got approved and are being used. And the original observation was you're seeing microinfarcts in the heart with these patients. So it's really like the fibrosis furnace. And then we looked more broadly at dystrophin deletions, and there also were fibrosis furnaces. So we said this is a place where a broad spectrum antifibrotic antibody may have a big impact. We started in the preclinical in 2005. We got cleared by the U.S.-EU board that reviews these things in 2014 for immediate human studies, and we moved straight ahead. We think there will be impact in both nonambulatory and in ambulatory. The evidence shows cardiovascular, pulmonary as well as muscle strength in the studies we're doing now. That date is going to come up pretty soon. So we're very excited about where that's going at the present time.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. Thank you for that. Unfortunately, we have run out of time at the moment, but we can continue the questions offline here with the management team off the stage. Thank you.

Thomas B. Neff

Founder, Chairman & CEO

Thank you, Paul.

K. Peony Yu

Chief Medical Officer
Thank you very much, Paul.

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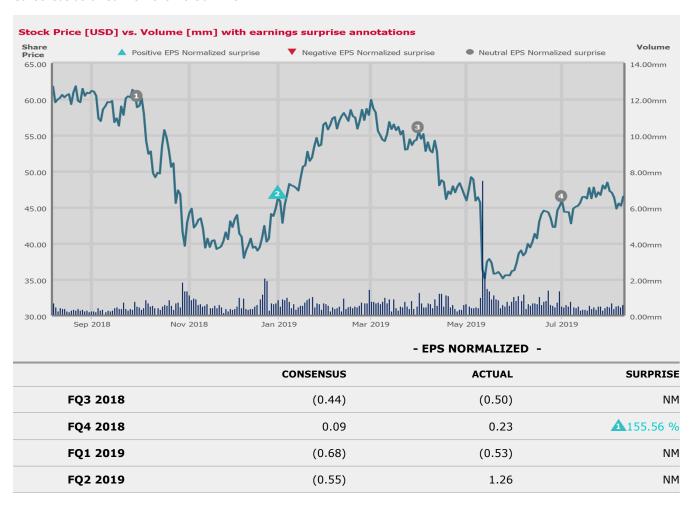
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S&P Global Market Intelligence Estimates

	-FQ2 2019-		-FQ3 2019-	-FY 2019-	-FY 2020-	
	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS	CONSENSUS	CONSENSUS
EPS Normalized	(0.55)	1.26	NM	(0.41)	(1.18)	(0.09)
Revenue (mm)	29.03	191.57	<u></u> 559.90	61.50	224.81	331.23

Currency: USD

Consensus as of Jul-25-2019 10:56 AM GMT



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Call Participants

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Presentation

Operator

Welcome to the FibroGen's Second Quarter 2019 Financial Results Conference Call. My name is Adrianne, and I'll be your operator for today's call. [Operator Instructions] Please note this conference is being recorded.

I'll now turn the call over to Karen Bergman. Karen Bergman, you may begin.

Karen L. Bergman

Vice President of Investor Relations & Corporate Communications

Thank you, Adrianne. Good afternoon, everyone. And thank you for joining our call. Today, we are reporting financial results and corporate update for the second quarter of 2019. Joining me today on the call are Mr. Tom Neff, Chairman and Chief Executive Officer; Dr. Peony Yu, Chief Medical Officer; Ms. Chris Chung, Senior Vice President of China Operations and Managing Director, FibroGen China; Dr. Elias Kouchakji, Senior Vice President, Clinical Development, Drug Safety and Pharmacovigilance; and Mr. Pat Cotroneo, Chief Financial Officer. Following our prepared remarks, Tom will discuss upcoming milestones and we will open the call to Q&A.

During this call, we may make forward-looking statements regarding our business, including our collaborations with AstraZeneca and Astellas; financial guidance; the initiation, enrollment, design, conduct and results of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities; and certain other business matters.

For risks and uncertainties regarding our business and statements made on the call today as well as factors beyond our control that may cause differences between current expectations and actual results, we refer you to our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, and to our quarterly report on Form 10-Q for the quarter ended June 30, 2019, filed with the Securities and Exchange Commission. Copies of these filings may be found in the Investors section of our website. We undertake no obligation to update any forward-looking statement whether as a result of our new information, future developments or otherwise.

The format for today's call includes remarks from FibroGen's management team, and then we'll open the lines to take your questions. The press release reporting our financial results and business update and a webcast of today's conference call can be found on the Investors section of FibroGen's website at www.fibrogen.com. The webcast will be available for 2 weeks from today's date.

And with that, I'd now like to turn the call over to our CEO, Tom Neff.

Thomas B. Neff

Founder, Chairman & CEO

Thank you, Karen. Welcome everyone, and thank you for joining us. Let's start with our anemia program. We are pleased to report that in our pre-NDA meeting with the FDA regarding roxadustat, we reached an agreement with the agency on the content of the NDA including the cardiovascular safety analysis. This is for both the dialysis and nondialysis dependent CKD populations. We previously announced that we expected the NDA submission in September or October time frame with the clarity arising from our meeting with FDA. We and our partner AstraZeneca have refined our timing to target an October submission, with the MAA for Europe to be submitted thereafter.

We recently announced the publication on July 24, 2 articles in The New England Journal of Medicine of the pivotal studies of roxadustat China Phase III program, 1 reporting the results from China Phase III dialysis or Study 806 and the other reporting the results from China Phase III nondialysis or Study 808. We view publication by the New England Journal of these 2 pivotal studies supporting regulatory approval for roxadustat in China's validation of the scientific and medical importance as well as the quality of clinical research for these studies.

Other updates in China, in December 2018, we announced the approval in China roxadustat for the treatment of CKD anemia and patients receiving dialysis representing the world's first approval for any HIF-PHI. We expect the nondialysis dependent or NDD portion of the CKD indication to be approved for roxadustat in the third quarter of 2019. In a few minutes Dr. Peony Yu will provide further details regarding roxadustat and Ms. Chris Chung will provide updates on China program.

Let's turn to pamrevlumab highlights for the quarter. Starting with Duchenne muscular dystrophy, we presented positive Phase II clinical findings from the first year of treatment in our ongoing study 079 at the Parent Project Muscular Dystrophy or PPMD 2019 Annual Conference in June. Our study suggests pamrevlumab has the potential treatment benefits on heart function, lung function and muscle function in DMD patients. We shall be seeking guidance from the FDA on the design of a Phase III program.

For the treatment of idiopathic pulmonary fibrosis or IPF, we initiated patient dosing in the ZEPHYRUS Phase III randomized, double-blind, placebo-controlled study of pamrevlumab with the primary endpoint of change of forced vital capacity or FVC over 52 weeks. We are enrolling more than 550 patients in this study and we expect to have more than 175 study sites globally.

Turning to pancreatic cancer. This disease is characterized by a high degree of growth of fibrosis characterized as desmoplasia, which is related to extensive CTGF expression. As an anti-CTGF agent, pamrevlumab has the potential to have a meaningful effect on pancreatic cancer. We are preparing to initiate patient dosing in the LAPIS study of Phase III randomized, double-blind, placebo-controlled study of pamrevlumab as a neoadjuvant therapy for patients with unresectable locally advanced pancreatic cancer or LAPC.

Later, on this call, Dr. Elias Kouchakji will discuss the DMD data presented at the PPMD conference and our IPF and pancreatic cancer Phase III trials in more detail. I have a few brief corporate and financial updates for the quarter. Our Chief Financial Officer, Pat Cotroneo, will provide further detail on finance later on the call. In the second quarter, we reported \$116 million in net income or \$1.34 per basic share or \$1.26 per diluted share in EPS. As of June 30, 2019, FibroGen had \$686.1 million in cash. We are privileged to welcome Ms. Suzanne Blaug as a member of FibroGen's Board of Directors. Suzanne is an experienced industry executive and advisor whose deep knowledge and critical commercial marketing and strategic planning experience will be invaluable as we advance our multiple late stage products.

I would now like to ask Dr. Peony Yu to provide updates on the anemia programs. Peony, please go ahead.

K. Peony Yu

Chief Medical Officer

Thank you, Tom. Roxadustat is the first HIF-PHI for treatment of CKD anemia. And it is the largest known CKD anemia program. More than 10,000 CKD patients from 50 countries participated in our global Phase III studies. Over 8,000 of these patients are included in the dialysis or nondialysis pool for MACE analysis for the US and MACE Plus analysis for Europe as primary cardiovascular safety endpoint.

As stated by our US partner AstraZeneca, our Phase III results confirmed the cardiovascular safety of roxadustat. Together with our partners, AstraZeneca and Astellas, we recently had a very good pre-NDA meeting with the FDA on roxadustat. We reached agreement with the FDA on our proposed pool MACE analysis in dialysis and in nondialysis. We are pleased with the agreement for nondialysis as it includes an approach to account for the differential dropout between roxadustat and placebo. With agreement on NDA content and format, we are moving as quickly as we can for a submission. We do have a large submission, at this time, we are targeting October of this year.

For Europe, we are working with Astellas, our EU partner, on MAA preparation based on the Phase III results in the roxadustat program. Astellas has recently updated MAA submission timeline from calendar year 2019 to their fiscal year 2019, which ends March 2020. We look forward to present Phase III study results in upcoming medical conferences such as ASN in November and in peer reviewed journals. In Japan, Astellas submitted NDA for roxadustat treatment of anemia in dialysis-dependent CKD patients in last September. The PMDA's regulatory decision on this NDA is expected this year.

We and our partners AstraZeneca and Astellas are working together on expanding anemia treatment beyond CKD. In MDS, we have 2 ongoing clinical studies, a Phase III US global study in transfusion-dependent MDS patients and a Phase II/III study in nontransfusion-dependent MDS patients in China. We are now starting a Phase II US study of roxadustat for treating chemotherapy-induced anemia on track for starting this quarter.

I now like to turn the call back over to Tom.

Thomas B. Neff

Founder, Chairman & CEO

Thank you, Peony. Next, I'd like to ask Chris Chung, who heads our China operations to offer some comments on roxadustat in China, our country of first approval. Chris, please go ahead.

Christine L. Chung

Senior Vice President of China Operations

Thanks, Tom. It's been a productive quarter on the China front. We have been projecting a Q3 commercialization date. Certification of our commercial API plant in Cangzhou, the gating factor, was achieved in May. I'm pleased to share the news with everyone that the first batches of commercial roxadustat capsules have been shipped. We all know that affordability for our patients is critical to widespread market adoption. Government reimbursement for roxadustat is something that we're actively pursuing, historically, as taken a number of years after NDA approval before a drug is reimbursed by the Chinese government.

We have made this as a base case assumption. Until we secure government reimbursement, the near-term market adoption rate will be slow. Nonetheless, we believe we have a strong case for roxadustat to be included for reimbursement sooner rather than later, given the scope of the unmet medical need, the novel treatment pathway, the strength of our clinical data and the fact that access to innovative medicines is a top national priority. It is still too early to tell if roxadustat will be included in the 2019 reimbursement cycle, but we should have more clarity by the end of this year.

If reimbursement is not obtained, we will have drug available for patients in the self-pay market, and our market development efforts with AstraZeneca will continue to advance. We remain highly optimistic about the market potential for roxadustat in China. We continue to build momentum [with our] investments in marketing, market access and medical affairs and the AstraZeneca field sales force is being scaled up to address the size of the market opportunity.

I look forward Tom to keeping everyone updated in the exciting months ahead. Now back to you, Tom.

Thomas B. Neff

Founder, Chairman & CEO

Thank you, Chris. Moving on to pamrevlumab, Dr. Elias Kouchakji will provide a few more details on the Phase II data update we recently presented at the PPMD Annual Conference in July, as well as the progress in our Phase III studies in IPF and LAPC. Elias, please go ahead.

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Thank you, Tom. I would like to start with our work in Duchenne muscular dystrophy. As Tom mentioned, we presented positive Phase II primary clinical data of the first full year of treatment in all 21 nonambulatory Duchenne muscular dystrophy patients at the PPMD 2019 Annual Conference in June, notably, on cardiac function fibrosis and muscle function.

It is important to note the decline in cardiac function is the leading cause of mortality in nonambulatory Duchenne muscular dystrophy. In this study, we showed an increase in estimated mean change from baseline and left ventricular ejection fraction, also known as LVF, of positive 0.29% versus what is in expected decline in LVF. Additionally, a correlation between improvement in LVF and reduction in cardiac fibrosis was presented. Neither of these results has been previously reported in scientific literature.

Speaking of the [indiscernible] nonambulatory Duchenne muscular dystrophy patient, we know this will eventually lead to the further reduction of their quality of life. The results of upper arm muscle function and muscle fibrosis patch showed mean change in pull from baseline of a decline of 1.53, demonstrating a potential meaningful reduction in the rate of the decline in comparison to the published data. Additionally, the results of estimated mean change in the grip strength score were positive and showed a score increase in both dominant and in nondominant hands at 1 year of treatment with pamrevlumab. The grip strengthen in this population typically is expected to decline. In this study, pamrevlumab was well tolerated. We are particularly excited by this result in the nonambulatory population, which to-date has been the subject of extremely limited clinical trials. We shall be seeking guidance from the FDA on the design of our Phase III program.

Moving to our program in IPF. We have initiated dosing in ZEPHYRUS Phase III study in IPF, a randomized, double-blind placebo-controlled Phase III clinical trial with the primary endpoints of a change in forced vital capacity, FVC, from baseline in approximately 565 patients to confirm efficacy and safety results we have seen in our Phase II studies. ZEPHYRUS Phase III study is similar in design to our Phase II placebo-controlled study, PRAISE. The objective is to confirm the positive efficacy and safety results previously reported in PRAISE, in which pamrevlumab treatment attenuated the progression of IPF and was well tolerated.

Last but not least, I will be turning to the pancreatic cancer study. We are screening patient for LAPIS Phase III study in pancreatic cancer, a randomized, double-blind, placebo-controlled Phase III study evaluating pamrevlumab as a neoadjuvant therapy for unresectable locally advanced pancreatic cancer. This study will enroll approximately 260 patients on standard of care. A standard of care is defined as a treatment to gemcitabine and nab-paclitaxel, and will be randomized to either pamrevlumab or placebo. In this study, we will be evaluating the rate of resection and overall survival. We believe that pamrevlumab can provide a new therapy to patient with IPF, LAPC and Duchenne muscular dystrophy, each of which are serious and fatal disease.

Thank you for listening and now I'll turn the call back to Tom.

Thomas B. Neff

Founder, Chairman & CEO

Thank you, Elias. Our Chief Financial Officer, Pat Cotroneo, will now walk through the financial results for the second quarter of 2019 and our financial outlook through fiscal year 2019. Pat, please proceed.

Pat Cotroneo

Senior VP of Finance & CFO

Thank you, Tom. As announced today, total revenue for the quarter ended June 30, 2019, was \$191.6 million as compared to \$44 million for the second quarter of 2018. For the same period, operating expenses were \$78.7 million and net income was \$116 million or \$1.34 per basic share and a \$1.26 per diluted share as compared to operating expenses of \$67.2 million and the net loss of \$23.4 million or \$0.28 per basic and diluted share for the second quarter last year.

Included in operating expenses for the quarter ended June 30, 2019, was an aggregate noncash portion totaling \$21.9 million, of which \$17.6 million was a result of stock-based compensation expense, as compared to an aggregate noncash portion totaling \$15.2 million, of which \$13.2 million was a result of stock-based compensation expense for the same period in the prior year.

In accordance with US GAAP, in the second quarter, we are including in our revenue recognition methodology a total of \$180 million comprised of \$50 million for an anticipated milestone from AstraZeneca relating to the filing of the US NDA and the \$130 million in anticipated milestones from Astellas in connection with the EU MAA filings. Out of the \$180 million, \$171.1 million was recognized in the current quarter and the remaining balance will be recognized in future periods. Under the current US GAAP revenue recognition guidelines, we are required to include estimated consideration from milestones in the determination of revenue recognition in the period that milestone achievement becomes probable.

The timing of when the payments related to these not milestones will be remitted to FibroGen depends upon when the milestones are actually achieved.

As noted earlier on this call, timing for the NDA filing is targeted for October of this year, and we expect the Astellas MAA submission to occur in the second half of the Astellas 2019 fiscal year with MAA filing in early 2020. Previously, we had reported as any cash range of \$720 million to \$730 million. Adjusting for our latest forecast, we would increase our 2019 ending cash estimate to \$740 million to \$750 million. Given that the milestone payments could move into next year, I'd like to provide additional scenarios. Assuming that the EU MAA filing is done and completed in 2020 and the \$130 million and associated milestones are paid at that time, our current anticipated ending 2019 cash range will be approximately \$610 million to \$620 million. This ending cash range assumption also includes a \$50 million milestone from AstraZeneca for the filing of the US NDA, which should occur within 60 days after NDA submission. At June 30, 2019, FibroGen had \$686.1 million in cash, restricted time deposits, cash equivalents, investments and receivables.

Thank you, and I would now like to turn the call back over to Tom.

Thomas B. Neff

Founder, Chairman & CEO

Thank you, Pat. Let's wrap up by pointing out to some key events ahead. For roxadustat in the US, we anticipate submitting our NDA -- to the US FDA for the treatment of anemia associated with dialysis-dependent and nondialysis-dependent CKD in October 2019. We expect the EU MAA to be submitted by our partner Astellas thereafter. In China, we expect to add nondialysis-dependent CKD patients to the roxadustat label in Q3 2019. We also expect to initiate our Phase II study of roxadustat for the treatment of chemotherapy-induced anemia in this quarter.

For pamrevlumab, we are pushing forward with 3 indications in the mid- to late-stage development and we are looking forward to keeping you updated on those activities including an IPF progression of our ZEPHYRUS Phase III IPF study and locally advanced pancreatic cancer or LAPC initiation and progression of our LAPIS Phase III study.

In DMD, having reported on the first year of treatment and our ongoing Phase II DMD study and now advancing our patients through their second third and fourth years of treatment, we plan to seek guidance from the FDA on the design of a Phase III program.

With that, let me turn this back to Karen to begin the question-and-answer session. Karen, please go ahead.

Karen L. Bergman

Vice President of Investor Relations & Corporate Communications Thank you, Tom. Adrianne, please open up the line for questions.

Question and Answer

Operator

[Operator Instructions]

Karen L. Bergman

Vice President of Investor Relations & Corporate Communications

We are set for our first question; I think it's from Michael Yee.

Michael Jonathan Yee

Jefferies LLC, Research Division

Two questions. One is for Tom, what were the 2 or 3 most important things that you guys discussed with the FDA or topics or key issues regarding approvability in your meeting? And then, separately, regarding the statistical plan, there seems to be a concern about noninferiority on MACE, not MACE Plus, but MACE. Can you talk to your confidence around the statistics and whether that's an issue for the FDA?

Thomas B. Neff

Founder, Chairman & CEO

Peony, go ahead.

K. Peony Yu

Chief Medical Officer

Hi, Mike. This is Peony. In the FDA meeting, we have accomplished what we intended for the meeting. You asked about the important agreement or achievement. I will name that. We have gained FDA's agreement on our proposal for a single primary safety cardiovascular endpoint analysis for dialysis, as well as cardiovascular safety primary endpoint for nondialysis.

And in terms of the way that the time to MACE primary endpoint is being analyzed in nondialysis, this will account for differential drop out between our drug and placebo, whereas you know that because placebo doesn't work in treating anemia, placebo patients had a tendency to drop out earlier. And we have reached agreement on statistical method that accounts for that. You have asked about our confidence on noninferiority on MACE. At this time, with these understanding, level of confidence is very high and we do believe as AstraZeneca has stated that our Phase III results confirm cardiovascular safety of roxadustat in the CKD population in both dialysis and nondialysis.

Thomas B. Neff

Founder, Chairman & CEO

And Mike, I would add that what I saw was that we gained a lot of clarity across the board and both our team and AZ's team reflected a very high degree of confidence coming out of the meeting. So, there is detailed planning right now, how to get everything done in October early and so everybody is aggressively moving ahead.

Operator

And the next question comes from Geoff Porges from SVB Leerink.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

And I have to ask some follow-up questions. Could you confirm whether you have written minutes from the meeting with the agency? And then, Peony, you mentioned the exposure adjusted analysis of the time to first MACE event but could you -- we haven't seen that analysis. But, presumably you have run it already. Can you tell us either what the absolute rates when you adjust for exposure between the 2 groups and nondialysis group or at least what range, where they are in terms of relation to each other?

And then, could you explain the amendment in your Q that the European regulator is going to look at MACE as well as MACE Plus. Is that the result of a conversation or meeting and does that make you less confident or any change to your confidence about the European application?

Thomas B. Neff

Founder, Chairman & CEO

Geoff let me deal with the last issue first. There's no back story on the MACE, MACE Plus for Europe that we're aware of. So I think just take at face value. Peony, go ahead and address Geoff's other questions please.

K. Peony Yu

Chief Medical Officer

Geoff, we had our FDA meeting towards the end of July. So usually it will take a little bit longer before we received a meeting minutes. What I'm reporting to you is based on our exchange with the FDA and there was sufficient clarity for us to be sharing what we had just said. Okay?

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Great, thanks.

Operator

And our next question comes from Joel Beatty from Citi.

Joel Lawrence Beatty

Citigroup Inc, Research Division

Recently at the end of July there was a New England Journal of Medicine publication and Phase III results from China. There was also an editorial in there that generally seems favorable, talked about hyperkalemia and the studies with a little bit of reservation. Would you be able to address that, the potential to use roxadustat in patients with hyperkalemia? And then, also discuss from the US EU Phase III results if that was a finding that seemed to show up?

Thomas B. Neff

Founder, Chairman & CEO

So, Joel, as a starting point here, the editorial work and such with these 2 articles for New England Journal was quite aggressive, intensive and so on, for about a month. And the topic of safety discussion came up right at the end at their editorial board's suggestion. So it was a little surprising. I think Peony can explain how we see it. Go ahead Peony.

K. Peony Yu

Chief Medical Officer

Thanks, Tom. That was intensive. So I believe that we had previously discussed hyperkalemia in or around November after ASN last year. And coming back to New England Journal, yes, it was reported that there was an apparent imbalance of hyperkalemia reported as adverse events by investigators in the 2 China Phase III studies. Now, New England Journal supplement for these 2 manuscripts also showed that there is no imbalance in the hyperkalemia when we reported the analysis based on central lab data. Just as a background on CKD patients, elevation of blood potassium level is consistent and characteristic of CKD patient populations, because the diseased kidneys are not able to properly regulate potassium levels and acid base balance.

To address your questions on the larger Phase III program that has been reported and that indeed is another -- is a good way to further look into this question. So, from what we have seen the reported incidence rates of hyperkalemia adverse events were comparable between roxadustat and comparator arms in the dialysis and the nondialysis studies. Also, the analysis of potassium central lab values also

suggests, there is a hyperkalemia risk with the use of roxadustat. We look forward to presenting the results from these much larger and longer Phase III studies in upcoming medical conferences.

Operator

And our next question comes from Difei Yang from Mizuho.

Difei Yang

Mizuho Securities USA LLC, Research Division

On the roxadustat NDA filing, would you remind us who's primarily responsible to submit the NDA, is it AstraZeneca or is it FibroGen?

Thomas B. Neff

Founder, Chairman & CEO

I will have Peony address this, please.

K. Peony Yu

Chief Medical Officer

Yes, AstraZeneca is a very good partner in the US. In terms of roles and responsibility, FibroGen is the IND holder. And we are also the party responsible for the final, putting together the file and submitting to the FDA. In terms of ways of working together, we have a highly collaborative relationship with both of our partners. And we have frequent communication as well as generating the study results together.

Difei Yang

Mizuho Securities USA LLC, Research Division

Now changing subject to IPF, you have started recruiting for the Phase III, would you remind us when should we be expecting top-line results?

Thomas B. Neff

Founder, Chairman & CEO

Elias, please go ahead.

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Difei, its Elias. We just started enrolling in this study. This study will have to enroll across a little bit over 550 patients. This is going to take a little time to enroll as we have seen in all IPF studies. When the last patient is enrolled and have a 1-year of treatment, this is what we consider the end of the study and at that time would be possibly can see this data between the late 2022 and early 2023.

Operator

And our next question comes from Adam Walsh from Stifel.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

This is Edwin on for Adam. Congrats again on the progress made in the last quarter. So I have a few questions, if I may. My first question is on incident dialysis. So what is your filing and commercial strategy over there? So based on the efficacy and safety data, do you expect this incident dialysis patient population will be defined and listed in the [indiscernible] label if approved. And similarly, can you also comment on the nondialysis setting? So what is your strategy and view there? And I have a follow up questions.

Thomas B. Neff

Founder, Chairman & CEO

Peony, you can address incident dialysis first.

K. Peony Yu

Chief Medical Officer

Okay. Thank you for the question, Adam.

Thomas B. Neff

Founder, Chairman & CEO

Not Adam. It's Edwin.

K. Peony Yu

Chief Medical Officer

Oh, Edwin. I'm sorry. So in terms of our submission, we are seeking approval for treating CKD anemia in our dialysis as the primary patient indicate -- as the primary indication and also nondialysis. Now for incident dialysis, we do believe that this is a very important subgroup in -- which is part of our dialysis. The reason that we say that and also have this discussion supported -- this discussion with our medical reviewer is that, oftentimes anemia therapy starts around the time of dialysis initiation and we continue to follow the patients during the course of treatment anemia drug as well as during the course of dialysis. And now given the importance of this information for prescribing physician, they do feel that information on the outcome of the incident dialysis patients are important to prescriber and we expect this to have positive impact on commercial potentials. Our FDA medical reviewer has suggested additional analysis and whether -- and as far as labeling that will be a review issue.

Thomas B. Neff

Founder, Chairman & CEO

The second question was about NDD, is that correct?

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

Yes.

Thomas B. Neff

Founder, Chairman & CEO

Okay. So Peony, please address NDD. Can you restate your full question for NDD?

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

Similar to the incident dialysis population, what is your filing and the commercial strategy? And also, maybe comment on the potential competition because you set a high bar in safety [indiscernible] to placebo.

Thomas B. Neff

Founder, Chairman & CEO

Peony, go ahead.

K. Peony Yu

Chief Medical Officer

Yes. So we are very pleased with the agreement on the primary safety analysis of our primary cardiovascular safety endpoint in NDD. We had -- because when we were considering the value of a drug whether from a medical point of view and commercial point of view is looking at benefit and risk. And we are very pleased with the positive efficacy results for anemia therapy not only just to keep hemoglobin level up, but also reduce blood transfusion risk as well as attenuation of renal progression that we have previously reported.

Now, on the safety side, the ability to demonstrate a drug is as safe as placebo, which is a very high bar because placebo is considered -- to give the drug an opportunity to show how safe it is based on its own merit. And the fact that our drug has a placebo comparator and also it is orally administered, which makes it accessible to patients, we believe that we will, or we will have an opportunity to address the unmet medical need and expand the market beyond what ESA is able to do as -- and we both we and our partner AstraZeneca believe that the nondialysis market is larger than that of the dialysis market.

Thomas B. Neff

Founder, Chairman & CEO

Potential market in nondialysis is larger than the current market in dialysis. I think we will probably decline to comment on the competitive aspects. Did you have any other questions?

Operator

He has left the queue.

Thomas B. Neff

Founder, Chairman & CEO

Thank you.

Operator

We do have a question from Danielle Brill from Piper Jaffray.

Nirav Y. Shelat

Piper Jaffray Companies, Research Division

This is Nirav on for Danielle. I just had 2, regarding a question that was asked earlier. I'm not sure if it was answered. Would you be able to tell us with the data that you currently have and this statistical analysis that you're doing with the absolute rates where, when you adjust for the drop outs?

Thomas B. Neff

Founder, Chairman & CEO

We won't be able to discuss that until later in the process.

Nirav Y. Shelat

Piper Jaffray Companies, Research Division

And the other question I had was regarding the IPF study. I was wondering with the enrollment currently ongoing, if you could give us some color on the geography of the sites? And how many sites are in the United States versus ex-US and if we should expect a significant amount of patients to come ex-US.

Thomas B. Neff

Founder, Chairman & CEO

These are targets now, we haven't accomplished this yet, so Elias, please go ahead and explain.

Elias Kouchakii

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Sure. The target is -- the majority would be from the US and this is globally as is other similar product, which is running globally. We are going in the EU and all other regions, Southeast and the potential number of patients coming from the US versus ex-US. We still are targeting to have a very large number from the patients who come from US at the same time. We are seeing this as a very good number of sites that are rolling and eager to be part of our study.

Operator

And this concludes the question-answer-session. I'll now turn the call back over to Tom Neff for final remarks.

Thomas B. Neff

Founder, Chairman & CEO

Let me say it's incredibly gratifying to see the advancement of roxadustat and pamrevlumab programs, and the recognition of their potential by the medical community as seen by the recent publications of our various clinical results. This is a testament to years of hard work on the part of our dedicated employees. We cannot thank enough to the patients and to their families and to physicians and to investigators, who are participating in our studies. We all have the same goal of expanding therapeutic options for patients who need them.

Thank you also to our shareholders, who have followed our story and are seeing the advancement and development of ideas born in our research lab. I'd like to wish everyone a good afternoon and evening. Thank you for joining our call.

Operator

Thank you, ladies and gentlemen. This concludes today's conference call. Thank you for participating and you may now disconnect.

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EXHIBIT O

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-Q

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☑ QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the quarterly period ended June 30, 2019

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to Commission file number: 001-36740

FIBROGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or Other Jurisdiction of Incorporation or Organization) 409 Illinois Street San Francisco, CA 77-0357827 (I.R.S. Employer Identification No.)

> 94158 (Zip Code)

(Address of Principal Executive Offices)

(415) 978-1200

Registrant's telephone number, including area code:

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which		
		registered		
Common Stock, \$0.01 par value	FGEN	The Nasdaq Global Select Market		

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes \square No \square

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (\S 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes \square No \square

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer	✓	Accelerated filer	
Non-accelerated filer		Smaller reporting company	
		Emerging growth company	

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. \Box

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2). Yes □ No ☑

The number of shares of common stock outstanding as of July 31, 2019 was 86,915,996.

FIBROGEN, INC.

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ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q, and in our Securities and Exchange Commission ("SEC") filings, including our Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on February 27, 2019.

FORWARD-LOOKING STATEMENTS

The following discussion and information contained elsewhere in this Quarterly Report on Form 10-Q contain "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended ("Exchange Act"), Section 27A of the Securities Act of 1933, as amended ("Securities Act") and within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "estimate," or "continue," and similar expressions or variations. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section titled "Risk Factors," set forth in Part II, Item 1A of this Quarterly Report on Form 10-Q. The forward-looking statements in this Quarterly Report on Form 10-Q represent our views as of the date of this Quarterly Report on Form 10-Q. We anticipate that subsequent events and developments will cause our views to change. New risks emerge from time to time, and it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this Quarterly Report on Form 10-Q may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. While we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Quarterly Report on Form 10-Q and are cautioned not to place undue reliance on such forward-looking statements.

BUSINESS OVERVIEW

We were incorporated in 1993 in Delaware and are headquartered in San Francisco, California, with subsidiary offices in Beijing and Shanghai, People's Republic of China ("China"), is a leading biopharmaceutical company discovering and developing a pipeline of first-in-class therapeutics. We apply our pioneering expertise in hypoxia-inducible factor ("HIF"), connective tissue growth factor ("CTGF") biology, and clinical development to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer. Roxadustat, our most advanced product candidate, is an oral small molecule inhibitor of HIF prolyl hydroxylase ("HIF-PH") activity, completing Phase 3 clinical development worldwide for the treatment of anemia in chronic kidney disease ("CKD"), with a New Drug Application ("NDA") now approved by the National Medical Products Administration ("NMPA") in China. We and our collaboration partners AstraZeneca AB ("AstraZeneca") and Astellas Pharma Inc. ("Astellas") are in the process of preparing an NDA for submission to the United States ("U.S.") Food and Drug Administration ("FDA") and a Marketing Authorization Application ("MAA") for submission to the European Medicines Agency ("EMA") this year. Astellas submitted an NDA for the treatment of anemia in CKD patients on dialysis in Japan in September 2018, which is currently under review by the Pharmaceuticals and Medical Devices Agency ("PMDA"). Roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes ("MDS"). Pamrevlumab, an anti-CTGF human monoclonal antibody, is in Phase 3 clinical development for the treatment of idiopathic pulmonary fibrosis ("IPF"), and advancing towards Phase 3 for the treatment of pancreatic cancer. Pamrevlumab is also currently in a Phase 2 trial for Duchenne muscular dystrophy ("DMD"). We are also developing a biosynthetic cornea in China.

Financial Highlights

	Three Months Ended June 30,			Six Months Ended June 30,				
	2019			2018		2019 t for per share data)		2018
				(in thousands, except	for			
Result of Operations								
Revenue	\$	191,566	\$	43,952	\$	215,429	\$	75,876
Operating expenses	\$	78,747	\$	67,193	\$	151,453	\$	139,717
Net income (loss)	\$	116,003	\$	(23,421)	\$	70,592	\$	(64,817)
Net income (loss) per share - basic	\$	1.34	\$	(0.28)	\$	0.82	\$	(0.78)
Net income (loss) per share - diluted	\$	1.26	\$	(0.28)	\$	0.77	\$	(0.78)
						June 30, 2019	De	cember 31, 2018
						(in tho	usand	ls)
Balance Sheet								
Cash and cash equivalents					\$	74,587	\$	89,258
Short-term and long-term investments					\$	597,089	\$	587,964
Accounts receivable					\$	6,453	\$	63,684

Our revenue for the three and six months ended June 30, 2019 increased compared to the same periods a year ago. Our revenue for the current year periods primarily consisted of the recognition of \$129.5 million of two regulatory milestones totaling \$130.0 million that were included in the transaction price during the second quarter of 2019 when these milestones became probable of being achieved. These milestones are associated with the planned MAA submission to the EMA under the collaboration agreement with Astellas for roxadustat as a treatment for dialysis and non-dialysis CKD patients. In addition, the revenue recognized during the current year periods included the recognition of \$41.6 million of a \$50.0 million regulatory milestone that was included in the transaction price during the second quarter of 2019 when this milestone became probable of being achieved. This milestone is associated with the planned NDA submission to the FDA under the collaboration agreement with AstraZeneca for roxadustat as a treatment for dialysis and non-dialysis CKD patients. As comparison, our revenue for the prior year period included the recognition of \$14.9 million of a \$15.0 million regulatory milestone associated with NDA submission in Japan under the collaboration agreement with Astellas for roxadustat for the treatment of anemia in Japan that was included in the transaction price during the second quarter of 2018 when this milestone became probable of being achieved. The increases were partially offset by a decrease in co-development billings related to the development of roxadustat as a result of the substantial completion of Phase 3 trials for roxadustat.

Operating expenses for the three months ended June 30, 2019 increased compared to the same period a year ago primarily due to \$9.2 million higher outside service expenses related to co-promotional activities and scientific contract expenses, \$4.4 million higher stock-based compensation related to the cumulative impact of stock option grant activities, \$2.6 million amortization of finance lease right-of-use ("ROU") assets related to the adoption of lease accounting guidance under Accounting Standards Codification ("ASC") 842 - Leases ("ASC 842") and \$1.1 million higher depreciation expenses due to the change in estimated useful life for our leasehold improvements as a result of the adoption of ASC 842. The increases were partially offset by \$3.4 million lower clinical trial expenses related to lower activities for roxadustat offset by higher activities for pamrevlumab, and \$2.5 million lower drug development expenses associated with drug substance manufacturing activities related to pamrevlumab.

Operating expenses for the six months ended June 30, 2019 increased compared to the same period a year ago primarily due to \$11.4 million higher outside service expenses related to co-promotional activities and scientific contract expenses, \$10.0 million higher stock-based compensation related to the cumulative impact of stock option grant activities, \$5.2 million amortization of finance lease ROU assets related to the adoption of lease accounting guidance under ASC 842, \$2.3 million higher depreciation expenses due to the change in estimated useful life for our leasehold improvements as a result of the adoption of ASC 842 and \$1.8 million higher employee-related expenses resulting from higher average compensation level. The increases were partially offset by \$11.7 million lower clinical trial expenses related to lower activities for roxadustat offset by higher activities for pamrevlumab, \$6.2 million lower drug development expenses associated with drug substance manufacturing activities related to pamrevlumab.

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During the three months ended June 30, 2019, we had a net income of \$116.0 million, or net income per basic share of \$1.34, and net income per diluted share of \$1.26, as compared to a net loss of \$23.4 million for the same period a year ago, due to an increase in revenue partially offset by an increase in operating expenses. During the six months ended June 30, 2019, we had a net income of \$70.6 million, or net income per basic share of \$0.82, and net income per diluted share of \$0.77, as compared to a net loss of \$64.8 million for the same period a year ago, due to an increase in revenue partially offset by an increase in operating expenses.

Cash and cash equivalents, investments and accounts receivable totaled \$678.1 million at June 30, 2019, a decrease of \$62.8 million from December 31, 2018, primarily due to the cash used in operations, partially offset by the accounts receivable at December 31, 2018 collected during the year.

Programs

Roxadustat for the Treatment of Anemia in Chronic Kidney Disease

Roxadustat is our most advanced product candidate, an oral small molecule inhibitor of HIF-PH activity that acts by stimulating the body's natural pathway of erythropoiesis, or red blood cell production. We received our first NDA approval in China for roxadustat for the treatment of anemia caused by CKD in dialysis patients in December of 2018.

We have reported top line efficacy data from individual studies and safety data for the pooled non-dialysis population and the pooled dialysis population, as well as the incident dialysis subpopulation, from the roxadustat Phase 3 trials intended to support our NDA in the U.S. and MAA in the European Union ("EU") for the treatment of anemia in CKD.

In our pre-NDA meeting with the FDA, we reached agreement on the content to be included in our NDA submission package for roxadustat for treatment of anemia in CKD, including the cardiovascular safety analyses for both CKD-dialysis and CKD-non-dialysis. The agreement for non-dialysis is an approach to account for the differential dropout between roxadustat and placebo observed in our Phase 3 studies. We are confident we have sufficient data for FDA review of our NDA in both CKD dialysis and CKD non-dialysis and we are planning to submit the NDA in October of 2019. Our partner Astellas is planning for an MAA submission to the EMA during the second half of their fiscal year 2019, which ends on March 31, 2020.

In China, we have secured regulatory approval of our commercial active pharmaceutical ingredient ("API") plant in Cangzhou, Hebei. We have subsequently produced commercial batches of API and shipped commercial drug product. Roxadustat is currently approved for the treatment of anemia in CKD patients on dialysis. We expect non-dialysis CKD patients to be added to the roxadustat label in the third quarter of 2019.

In Japan, Astellas submitted an NDA for roxadustat for the treatment of anemia in CKD patients on dialysis in September 2018, which is currently under review by the PMDA. We expect an approval decision on the Japan dialysis NDA in the second half of 2019. Astellas has announced it expects the second non-dialysis study in Japan to be completed in 2019.

Roxadustat for the Treatment of Anemia in Myelodysplastic Syndromes

In addition to anemia in CKD, we are continuing to enroll the 156-patient double-blind, placebo-controlled portion of our global Phase 3 clinical study of roxadustat in transfusion-dependent, lower risk MDS patients. The primary endpoint is the proportion of patients who achieve transfusion independence.

In China, we continue to enroll the open-label portion of our Phase 2/3 clinical trial to evaluate the safety and efficacy of roxadustat in non-transfusion dependent, lower risk MDS patients with anemia. After the open-label portion we expect to begin the 135-patient double-blind, placebo-controlled Phase 3 portion of the study, in which subjects will be randomized 2:1 to receive roxadustat or placebo three-times weekly for 26 weeks. The primary endpoint for this study is percentage of patients achieving a hemoglobin response.

Roxadustat for the Treatment of Anemia in Chemotherapy Induced Anemia

We plan to initiate a Phase 2 clinical trial of roxadustat in the U.S. in chemotherapy induced anemia in the third quarter of 2019.

Pamrevlumab (FG-3019) - Monoclonal Antibody Against Connective Tissue Growth Factor (CTGF)

Pamrevlumab is our human monoclonal antibody that inhibits the activity of CTGF, a central mediator and critical common element in the progression of fibrotic and fibro-proliferative diseases. We initiated our Phase 3 clinical trial of pamrevlumab for the treatment of IPF and are screening patients in our Phase 3 clinical trial for locally advanced unresectable pancreatic cancer. We recently presented topline results from our 1-year data from our ongoing Phase 2 trial for DMD.

In the U.S., pamrevlumab has received orphan drug designation for DMD in addition to IPF and pancreatic cancer, and Fast Track designation for the treatment of both IPF patients and patients with locally advanced unresectable pancreatic cancer from the FDA.

Idiopathic Pulmonary Fibrosis

We recently began enrolling ZEPHYRUS, our double-blind, placebo-controlled Phase 3 trial of pamrevlumab in approximately 565 IPF patients. This study is powered to meet the FDA requirement of a highly statistically-significant result in the primary efficacy endpoint of change from baseline in forced vital capacity ("FVC").

Locally Advanced Unresectable Pancreatic Cancer

We are actively screening patients for LAPIS, our double-blind placebo controlled Phase 3 trial of pamrevlumab as a neoadjuvant therapy for locally advanced unresectable pancreatic cancer. We intend to enroll approximately 260 patients, randomized 1:1 to receive either pamrevlumab, in combination with gemcitabine and nab-paclitaxel, or placebo with gemcitabine and nab-paclitaxel.

Duchenne Muscular Dystrophy

In DMD, all 21 non-ambulatory patients from our fully enrolled Phase 2 open-label single-arm trial have completed over one year of treatment with pamrevlumab. While we cannot make direct comparisons between our trial and previously published data due to, among other things, differences in subject numbers, baseline characteristics, inclusion/exclusion criteria, treatment protocols, and analysis methods, we are encouraged by the data obtained so far. Pamrevlumab was well tolerated in this study.

In June 2019 at the Parent Project Muscular Dystrophy meeting, we reported topline results from our one-year administrative analysis comparing our Phase 2 data to recent published natural disease history studies of DMD patients.

In pulmonary function tests, the results from our study indicate a potential reduction in the 1-year decline in FVC percent predicted from baseline for our pamrevlumab-treated patients when compared to FVC data of DMD patients (whether such patients were taking steroids or not) published in 2019 by Ricotti. In the 2019 Ricotti study, the DMD patients were not taking any active drug (other than steroids). All of the patients in our Phase 2 pamrevlumab trial were taking steroids. In addition, pamrevlumab showed less decline in both percent predicted forced expiratory volume as compared to previously published study results of Meier in 2016, and in percent predicted peak expiratory flow rate, compared to what was observed in the study by Ricotti in 2019.

Our data showed an increase in cardiac function, measured by mean change of left ventricular ejection fraction ("LVEF"), of 0.29% from baseline for our pamrevlumab-treated patients. Whereas, data published in 2018 by McDonald of DMD patients only on steroids showed a mean LVEF decline of 0.82% from baseline in one year. In a sub-group analysis of pamrevlumab subjects with baseline LVEF greater than 50%, the mean change was an increase in LVEF of 1.79% from baseline.

In muscle function tests, the majority of the results of this Phase 2 study showed the mean change from baseline in our pamrevlumab-treated patients were more favorable than previously published data. Our results showed a positive increase in grip-strength score in both dominant and non-dominant hands at one year of treatment with pamrevlumab, while earlier results from a 2015 study by Seferian showed a decline at one year as expected. In the performance of the upper limb ("PUL") test specifically developed for DMD patients, our pamrevlumab-treated patients had a mean change from baseline of -1.53. In the 2019 study by Ricotti of DMD patients taking either nothing or only steroids, the annual mean change in the PUL test was -4.13. Furthermore, in our study a strong correlation between change in biceps brachii T2-mapping and change in PUL score was observed, demonstrating stabilization and even possible improvement in the muscle fibrosis burden.

Based on our administrative analysis and advice we received from expert advisors, we are planning to share these results with the FDA to discuss pivotal study design in our clinical development plan for DMD.

Collaboration Partnerships for Roxadustat

Our current and future research, development, manufacturing and commercialization efforts with respect to roxadustat and our other product candidates currently in development depend on funds from our collaboration agreements with Astellas and AstraZeneca as described below.

Astellas

In June 2005, we entered into a collaboration agreement with Astellas for the development and commercialization (but not manufacture) of roxadustat for the treatment of anemia in Japan ("Japan Agreement"). In April 2006, we entered into the Europe Agreement with Astellas for roxadustat for the treatment of anemia in Europe, the Commonwealth of Independent States, the Middle East, and South Africa. Under these agreements, we provide Astellas the right to develop and commercialize roxadustat for anemia indications in these territories.

We share responsibility with Astellas for clinical development activities required for the U.S. and the EU regulatory approval of roxadustat, and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will own and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

The Astellas agreements will continue in effect until terminated. Either party may terminate the agreements for certain material breaches by the other party. In addition, Astellas will have the right to terminate the agreements for certain specified technical product failures, upon generic sales reaching a particular threshold, upon certain regulatory actions, or upon our entering into a settlement admitting the invalidity or unenforceability of our licensed patents. Astellas may also terminate the agreements for convenience upon advance written notice to us. In the event of any termination of the agreements, Astellas will transfer and assign to us the regulatory filings for roxadustat and will assign or license to us the relevant trademarks used with the products in the Astellas territories. Under certain terminations, Astellas is also obligated to pay us a termination fee.

Consideration under these agreements includes a total of \$360.1 million in upfront and non-contingent payments, and milestone payments totaling \$557.5 million, of which \$542.5 million are development and regulatory milestones and \$15.0 million are commercial-based milestones. Total consideration, excluding development cost reimbursement and product sales-related payments, could reach \$917.6 million. The aggregate amount of such consideration received through June 30, 2019 totals \$487.6 million. Additionally, under these agreements, Astellas pays 100% of the commercialization costs in its territories. Astellas will pay us a transfer price, based on net sales, in the low 20% range for our manufacture and delivery of roxadustat.

During the second quarter of 2019, we received positive topline results from analyses of pooled major adverse cardiac event ("MACE") and MACE+ data from its Phase 3 trials evaluating roxadustat as a treatment for dialysis and non-dialysis CKD patients, enabling Astellas to prepare for an MAA submission to the EMA during their fiscal year 2019, which ends on March 31, 2020, following our planned NDA submission to the FDA anticipated in October of 2019. We evaluated the two regulatory milestone payments associated with the planned MAA submission and concluded that these milestones became probable of being achieved in the second quarter of 2019. Accordingly, the total consideration of \$130.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the Europe Agreement in the second quarter of 2019.

In addition, as of June 30, 2019, Astellas had separate investments of \$80.5 million in the equity of FibroGen, Inc.

AstraZeneca

In July 2013, we entered into the U.S./RoW Agreement, a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in the U.S. and all territories not previously licensed to Astellas, except China. In July 2013, through our China subsidiary and related affiliates, we entered into the China Agreement, a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in China. Under these agreements we provide AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories. We share responsibility with AstraZeneca for clinical development activities required for U.S. regulatory approval of roxadustat.

In 2015, we reached the \$116.5 million cap on our initial funding obligations (during which time we shared 50% of the joint initial development costs), therefore all development and commercialization costs for roxadustat for the treatment of anemia in CKD in the U.S., Europe, Japan and all other markets outside of China have been paid by Astellas and AstraZeneca since reaching the cap.

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In China, FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") will conduct the development work for CKD anemia, will hold all of the regulatory licenses issued by China regulatory authorities, and will be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is also responsible for 100% of development expenses in all other licensed territories outside of China. Outside of China, we are responsible, through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the AstraZeneca agreements.

Under the AstraZeneca agreements, we will receive upfront and subsequent non-contingent payments totaling \$402.2 million. Potential milestone payments under the agreements total \$1.2 billion, of which \$571.0 million are development and regulatory milestones and \$652.5 million are commercial-based milestones. Total consideration under the agreements, excluding development cost reimbursement, transfer price payments, royalties and profit share, could reach \$1.6 billion. The aggregate amount of such consideration received through June 30, 2019 totals \$444.2 million.

Under the U.S./RoW Agreement, AstraZeneca will pay for all commercialization costs in the U.S. and RoW and AstraZeneca will be responsible for the U.S. commercialization of roxadustat, with FibroGen undertaking specified promotional activities in the end-stage renal disease segment in the U.S. In addition, we will receive a transfer price for delivery of commercial product based on a percentage of net sales in the low- to mid-single digit range and AstraZeneca will pay us a tiered royalty on net sales of roxadustat in the low 20% range.

Under the China Agreement, which is conducted through FibroGen China Anemia Holdings, Ltd. ("FibroGen China"), the commercial collaboration is structured as a 50/50 profit share. AstraZeneca will conduct commercialization activities in China as well as serve as the master distributor for roxadustat and fund roxadustat launch costs in China until FibroGen Beijing has achieved profitability. At that time, AstraZeneca will recoup 50% of their historical launch costs out of initial roxadustat profits in China.

Payments under these agreements include over \$500.0 million in upfront, non-contingent and other payments received or expected to be received prior to the first U.S. approval, excluding development expense reimbursement.

AstraZeneca may terminate the U.S./RoW Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon 180 days prior written notice at will. If AstraZeneca terminates the U.S./RoW Agreement at will, in addition to any unpaid non-contingent payments, it will be responsible for paying for a substantial portion of the post-termination development costs under the agreed development plan until regulatory approval.

AstraZeneca may terminate the China Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon advance prior written notice at will. If AstraZeneca terminates our China Agreement at will, it will be responsible for paying for transition costs as well as make a specified payment to FibroGen China.

In the event of any termination of the agreements, but subject to modification upon termination for technical product failure, AstraZeneca will transfer and assign to us any regulatory filings and approvals for roxadustat in the affected territories that they may hold under our agreements, grant us licenses and conduct certain transition activities.

As mentioned above, during the second quarter of 2019, we received positive topline results from analyses of pooled MACE and MACE+ data from its Phase 3 trials for roxadustat, enabling our NDA submission to the FDA, which is anticipated in the third quarter of 2019. We evaluated the regulatory milestone payment associated with this planned NDA submission and concluded that this milestone became probable of being achieved in the second quarter of 2019. Accordingly, the consideration of \$50.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the U.S./ RoW Agreement in the second quarter of 2019.

Additional Information Related to Collaboration Agreements

Total cash consideration received through June 30, 2019 and potential cash consideration, other than development cost reimbursement, transfer price payments, royalties and profit share, pursuant to our existing collaboration agreements are as follows:

		Cash Received Through June 30,2019		Additional Potential Cash Payments (in thousands)	Total Potential Cash Payments		
Astellasrelated-party:							
Japan Agreement		77,593	\$	95,000	\$	172,593	
Europe Agreement		410,000		335,000		745,000	
Total Astellas		487,593		430,000		917,593	
AstraZeneca:							
U.S. / RoW Agreement		389,000		860,000		1,249,000	
China Agreement		55,200		321,500		376,700	
Total AstraZeneca		444,200		1,181,500		1,625,700	
Total revenue	\$ 9		\$	1,611,500	\$	2,543,293	

These collaboration agreements also provide for reimbursement of certain fully burdened research and development costs as well as direct out of pocket expenses.

RESULTS OF OPERATIONS

Revenue

	Three Mor	nths Ended	Six Months Ended								
	June	June 30,		nge	June	e 30,	Change				
	2019	2019 2018		%	2019	2018	\$	%			
	·			(dollars in thousands)							
Revenue:											
License revenue	\$ 150,581	\$ 14,323	\$ 136,258	951 %	\$ 150,581	\$ 14,323	\$ 136,258	951 %			
Development and other revenue	40,985	29,629	11,356	38 %	64,848	61,553	3,295	5 %			
Total revenue	\$ 191,566	\$ 43,952	\$ 147,614	336 %	\$ 215,429	\$ 75,876	\$ 139,553	184 %			

Our revenue to date has been generated substantially from our collaboration agreements with Astellas and AstraZeneca.

Under our revenue recognition policy, license revenue includes amounts from upfront, non-refundable license payments and amounts allocated pursuant to the standalone selling price method from other consideration received during the periods. This revenue is generally recognized as deliverables are met and services are performed.

Development revenue include co-development and other development related services. Co-development services are recognized as revenue in the period in which they are billed to our partners, excluding China. For China co-development services, revenue is deferred until the end of the development period once all performance obligations have been satisfied. Other development related services are recognized as revenue over the non-contingent development period, ranging from 36 to 89 months, based on a proportional performance method. Other revenues consist of sales of research and development material and have been included with Development and other revenue in the condensed consolidated statements of operations, as they have not been material for any of the periods presented.

PART II-OTHER INFORMATION

ITEM 1, LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below in addition to the other information included or incorporated by reference in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

We have marked with an asterisk (*) those risks described below that reflect substantive changes from the risks described under Part I, Item 1A "Risk Factors" included in our Annual Report on Form 10-K for the year ended December 31, 2018.

Risks Related to Our Financial Condition and History of Operating Losses

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or sustain profitability. We may require additional financings in order to fund our operations.*

We are a clinical-stage biopharmaceutical company with two lead product candidates in clinical development, roxadustat in anemia in chronic kidney disease ("CKD") and myelodysplastic syndromes ("MDS"), and pamrevlumab (FG-3019) in idiopathic pulmonary fibrosis ("IPF"), pancreatic cancer and Duchenne muscular dystrophy ("DMD"). Pharmaceutical product development is a highly risky undertaking. To date, we have focused our efforts and most of our resources on hypoxia-inducible factor ("HIF") and fibrosis biology research, as well as developing our lead product candidates. We are not profitable and, other than in 2006 and 2007 due to income received from our Astellas Pharma Inc. ("Astellas") collaboration, have incurred annual losses each year since our inception. We have not generated any revenue based on commercial drug product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss for the year ended December 31, 2018 was approximately \$86.4 million, and our net loss for the years ended December 31, 2017, and 2016, recast from amounts previously reported due to the adoption of the new revenue standards, were approximately \$120.9 million and \$58.1 million, respectively. As of June 30, 2019, we had an accumulated deficit of \$637.2 million. As of June 30, 2019, we had capital resources consisting of cash, cash equivalents and short-term investments of \$660.8 million plus \$10.9 million of long-term investments classified as available for sale securities. Despite contractual development and cost coverage commitments from our collaboration partners, AstraZeneca AB ("AstraZeneca") and Astellas, and the potential to receive milestone and other payments from these partners, and despite our expectation to launch commercialization efforts in China for roxadustat for the treatment of anemia caused by CKD in dialysis patients, we anticipate we will continue to incur losses for the foreseeable future, and we anticipate these losses will increase as we continue our development of and seek regulatory approval for our product candidates and in our commercialization efforts. If we do not successfully develop and obtain regulatory approval for our existing or any future product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales, and even if we do generate product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

We believe that we will continue to expend substantial resources for the foreseeable future as we continue late-stage clinical development of roxadustat, grow our operations in the People's Republic of China ("China"), expand our clinical development efforts on pamrevlumab, seek regulatory approval, prepare for the commercialization of our product candidates, and pursue additional indications. These expenditures will include costs associated with research and development, conducting preclinical trials and clinical trials, obtaining regulatory approvals in various jurisdictions, and manufacturing and supplying products and product candidates for ourselves and our partners. In particular, in our planned Phase 3 clinical trial program for roxadustat, which we believe will be the largest Phase 3 program ever conducted for an anemia product candidate, we are expecting to enroll more than 8,000 patients for our United States ("U.S.") and European programs alone. We are conducting this Phase 3 program in conjunction with Astellas and AstraZeneca, and we are substantially dependent on Astellas and AstraZeneca for the funding of this large program. The outcome of any clinical trial and/or regulatory approval process is highly uncertain and we are unable to fully estimate the actual costs necessary to successfully complete the development and regulatory approval process for our compounds in development and any future product candidates. We believe that the net proceeds from our 2017 public offerings, our existing cash and cash equivalents, short-term and longterm investments and accounts receivable, and expected third party collaboration revenues will allow us to fund our operating plans through at least the next 12 months. Our operating plans or third party collaborations may change as a result of many factors, which are discussed in more detail below, and other factors that may not currently be known to us, and we therefore may need to seek additional funds sooner than planned, through offerings of public or private securities, debt financings or other sources, such as royalty monetization or other structured financings. Such financings may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. We may also seek additional capital due to favorable market conditions or strategic considerations even if we currently believe that we have sufficient funds for our current or future operating plans.

Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress in the development of our product candidates;
- the costs of development efforts for our product candidates, such as pamrevlumab, that are not subject to reimbursement from our collaboration partners;
- the costs necessary to obtain regulatory approvals, if any, for our product candidates in the U.S., China and other jurisdictions, and
 the costs of post-marketing studies that could be required by regulatory authorities in jurisdictions where approval is obtained;
- the continuation of our existing collaborations and entry into new collaborations;
- the time and unreimbursed costs necessary to commercialize products in territories in which our product candidates are approved for sale:
- the revenues from any future sales of our products as well as revenue earned from profit share, royalties and milestones;
- the level of reimbursement or third party payor pricing available to our products;
- the costs of establishing and maintaining manufacturing operations and obtaining third party commercial supplies of our products, if any, manufactured in accordance with regulatory requirements;
- · the costs we incur in maintaining domestic and foreign operations, including operations in China;
- regulatory compliance costs;
- · the costs of our commercialization efforts for roxadustat for the treatment of anemia caused by CKD in dialysis patients in China; and
- the costs we incur in the filing, prosecution, maintenance and defense of our extensive patent portfolio and other intellectual property rights.

Additional funds may not be available when we require them, or on terms that are acceptable to us. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations or activities that may be necessary to commercialize our product candidates.

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All of our recent revenue has been earned from collaboration partners for our product candidates under development.

Substantially all of our revenues recognized in recent years have been from our collaboration partners.

We will require substantial additional capital to achieve our development and commercialization goals, which for our lead product candidate, roxadustat, is currently contemplated to be provided under our existing third party collaborations with Astellas and AstraZeneca.

If either or both of these collaborations were to be terminated, we could require significant additional capital in order to proceed with development and commercialization of our product candidates, including with respect to our expected commercialization for roxadustat for the treatment of anemia caused by CKD in dialysis patients in China, or we may require additional partnering in order to help fund such development and commercialization. If adequate funds or partners are not available to us on a timely basis or on favorable terms, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations.

If we are unable to continue to progress our development efforts and achieve milestones under our collaboration agreements, our revenues may decrease and our activities may fail to lead to commercial products.

Substantially all of our revenues to date have been, and a significant portion of our future revenues are expected to be, derived from our existing collaboration agreements. Revenues from research and development collaborations depend upon continuation of the collaborations, reimbursement of development costs, the achievement of milestones and royalties and profits from our product sales, if any, derived from future products developed from our research. If we are unable to successfully advance the development of our product candidates or achieve milestones, revenues under our collaboration agreements will be substantially less than expected.

Risks Related to the Development and Commercialization of Our Product Candidates

We are substantially dependent on the success of our lead product candidate, roxadustat, and our second compound in development, pamreylumab.*

To date, we have invested a substantial portion of our efforts and financial resources in the research and development of roxadustat and pamrevlumab. While we have received approval of our New Drug Application ("NDA") for roxadustat in China for CKD anemia in dialysis patients, we will need to make substantial additional investments in both the development and commercialization of roxadustat worldwide and in various indications. Our near-term prospects, including maintaining our existing collaborations with Astellas and AstraZeneca, will depend heavily on successful development and commercialization of roxadustat, including obtaining regulatory approvals for the commercialization of roxadustat for anemia associated with CKD in the U.S., Europe, and Japan.

Our other lead product candidate, pamrevlumab, is currently in clinical development for IPF, pancreatic cancer and DMD. Pamrevlumab requires substantial further development and investment. We do not have a collaboration partner for support of this compound, and, while we have promising open-label safety data and potential signals of efficacy, we would need to complete larger and more extensive controlled clinical trials to validate the results to date in order to continue further development of this product candidate. In addition, although there are many potentially promising indications beyond IPF, pancreatic cancer and DMD, we are still exploring indications for which further development of, and investment for, pamrevlumab may be appropriate. Accordingly, the costs and time to complete development and related risks are currently unknown. Moreover, pamrevlumab is a monoclonal antibody, which may require experience and expertise that we may not currently possess as well as financial resources that are potentially greater than those required for our small molecule lead compound, roxadustat.

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, many of which are beyond our control, and we may be unable to complete the development or commercialization of roxadustat or pamrevlumab.*

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, including the following:

- the timely completion of data analyses from our Phase 3 clinical trials for roxadustat, which will depend substantially upon requirements for such trials imposed by the U.S. Food and Drug Administration ("FDA") and other regulatory agencies and bodies and the continued commitment and coordinated and timely performance by our third party collaboration partners, AstraZeneca and Astellas;
- the timely initiation and completion of our clinical trials for pamrevlumab, including in IPF, pancreatic cancer and DMD;
- our ability to demonstrate the safety and efficacy of our product candidates to the satisfaction of the relevant regulatory authorities;

- the ultimate approval criteria (which may include non-inferiority margins and statistical analyses methods), indications, patient populations, and ultimate benefit-risk analysis used by regulatory authorities in their approval processes;
- whether we are required by the FDA or other regulatory authorities to conduct additional clinical trials, and the scope and nature of such clinical trials, prior to approval to market our products;
- the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities, including pricing and reimbursement determinations:
- the ability to successfully commercialize our product candidates, if approved, for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;
- our ability and the ability of our third party manufacturing partners to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability;
- our success in educating health care providers and patients about the benefits, risks, administration and use of our product candidates, if approved;
- acceptance of our product candidates, if approved, as safe and effective by patients and the healthcare community;
- the success of efforts to enter into relationships with large dialysis organizations involving the administration of roxadustat to dialysis patients;
- the achievement and maintenance of compliance with all regulatory requirements applicable to our product candidates;
- the maintenance of an acceptable safety profile of our products following any approval;
- the availability, perceived advantages, relative cost, relative safety, and relative efficacy of alternative and competitive treatments;
- our ability to obtain and sustain an adequate level of pricing or reimbursement for our products by third party payors;
- our ability to enforce successfully our intellectual property rights for our product candidates and against the products of potential competitors; and
- our ability to avoid or succeed in third party patent interference or patent infringement claims.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we will ever be able to achieve profitability through the sale of, or royalties from, our product candidates. If we or our collaboration partners are not successful in obtaining approval for and commercializing our product candidates, or are delayed in completing those efforts, our business and operations would be adversely affected.

If our commercialization efforts for roxadustat in China are unsuccessful, our business, financial condition and results of operations will be materially harmed.

We have invested and continue to invest a significant portion of our efforts and financial resources in the development, approval and now commercialization of roxadustat for the treatment of anemia caused by CKD in dialysis patients in China, as well as in other indications and other geographic regions. With the marketing authorization received from the National Medical Products Administration ("NMPA") of roxadustat for the treatment of anemia caused by CKD in dialysis patients in China, we plan to launch commercialization efforts in China in the third quarter of 2019 with our commercialization partner AstraZeneca.

Our success of commercialization of roxadustat in China will depend on numerous factors in China, including:

- · our success in the marketing, sales, and distribution of the product along with our collaboration partner AstraZeneca;
- our success in negotiating a cost effective reimbursed price with the government in China;
- acceptance of roxadustat by state-owned and state-controlled hospitals, physicians, patients and the healthcare community;
- acceptance of pricing and placement of roxadustat on China's Medical Insurance Catalogs. Refer to "Business Government Regulation - Regulation in China";
- successfully establishing and maintaining commercial manufacturing with third parties;

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- successfully manufacturing our drug substances and drug products through our subsidiary FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing");
- receiving market authorization for roxadustat for anemia caused by CKD in non-dialysis patients;
- our success in arranging for and passing the inspection of our clinical sites by the NMPA;
- whether AstraZeneca is able to recruit and retain adequate numbers of effective sales and marketing personnel for the sale of roxadustat;
- whether we can compete successfully as a new entrant in the treatment of anemia caused by CKD in dialysis patients in China; and
- whether we will maintain sufficient funding to cover the costs and expenses associated with creating and sustaining a capable sales and marketing organization and related commercial infrastructure.

Successful commercialization of roxadustat will require significant resources and time, and there is a risk that we may not successfully commercialize roxadustat. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize roxadustat and generate revenues, which would deprive us from additional working capital and would materially harm our business. If we do not successfully commercialize roxadustat in China, our collaboration partners and third parties may also lose confidence in our ability to execute in commercialization efforts and become less likely to collaborate with us, and our business may be harmed.

As a Company, we have no commercialization experience, and the time and resources to develop such experience are significant. If we fail to achieve and sustain commercial success for roxadustat in China, either directly or with AstraZeneca, our business would be harmed.

Commercializing roxadustat in China with AstraZeneca will require us to establish commercialization systems, including but not limited to, medical affairs, sales, pharmacovigilance, supply-chain, and distribution capabilities to perform our portion of the collaborative efforts. These efforts will require resources and time. In particular, significant resources may be necessary to successfully market, sell and distribute roxadustat to patients with anemia caused by CKD in dialysis patients. If we, along with AstraZeneca, are not successful in setting our marketing, pricing and reimbursement strategy, facilitating adoption by hospitals in China, recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing roxadustat, which would adversely affect our business and financial condition.

As we evolve from a company primarily involved in research and development to a company potentially involved in commercialization, we may encounter difficulties in managing our growth and expanding our operations successfully.

If we are successful in advancing roxadustat and our other product candidates through the development stage towards commercialization, we will need to expand our organization, including adding marketing and sales capabilities or continuing to contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will also need to manage our existing and additional relationships with various collaborative partners, suppliers and other third parties. Future growth will impose significant added responsibilities on our organization, in particular on management. Our future financial performance and our ability to commercialize roxadustat and our other product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we may not be able to manage our growth efforts effectively, and hire, train and integrate additional management, administrative and sales and marketing personnel, and our failure to accomplish any of these activities could prevent us from successfully growing our Company.

Although FibroGen Beijing obtained regulatory approval for roxadustat in China in December 2018, we may be unable to obtain regulatory approval for our product candidates in other countries, or such approval may be delayed or limited, due to a number of factors, many of which are beyond our control.

The clinical trials and the manufacturing of our product candidates are and will continue to be, and the marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to develop and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical trials and clinical trials that the product candidate is safe and effective for use in each indication for which approval is sought. The regulatory review and approval process is expensive and requires substantial resources and time, and in general very few product candidates that enter development receive regulatory approval. In addition, our collaboration partners for roxadustat have final control over development decisions in their respective territories and they may make decisions with respect to development or regulatory authorities that delay or limit the potential approval of roxadustat, or increase the cost of development or commercialization. Accordingly, we may be unable to successfully develop or commercialize roxadustat or pamerelumab or any of our other product candidates.

Even though FibroGen Beijing obtained regulatory approval for roxadustat in China, we have not obtained regulatory approval for any of our product candidates in other countries and it is possible that roxadustat and pamrevlumab will never receive regulatory approval in other countries. Other regulatory authorities may take actions or impose requirements that delay, limit or deny approval of roxadustat or pamrevlumab for many reasons, including, among others:

- our failure to adequately demonstrate to the satisfaction of regulatory authorities that roxadustat is safe and effective in treating anemia in CKD or that pamrevlumab is safe and effective in treating IPF, pancreatic cancer or DMD;
- our failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the determination by regulatory authorities that additional clinical trials are necessary to demonstrate the safety and efficacy of roxadustat or pamrevlumab, or that ongoing clinical trials need to be modified in design, size, conduct or implementation;
- our product candidates may exhibit an unacceptable safety signal as they advance through clinical trials, in particular controlled Phase 3 trials;
- the clinical research organizations ("CROs") that conduct clinical trials on our behalf may take actions outside of our control that materially adversely impact our clinical trials;
- we or third party contractors manufacturing our product candidates may not maintain current good manufacturing practices ("cGMP"), successfully pass inspection or meet other applicable manufacturing regulatory requirements;
- regulatory authorities may not agree with our interpretation of the data from our preclinical trials and clinical trials;
- · collaboration partners may not perform or complete their clinical programs in a timely manner, or at all; or
- principal investigators may determine that one or more serious adverse events ("SAEs"), is related or possibly related to roxadustat, and any such determination may adversely affect our ability to obtain regulatory approval, whether or not the determination is correct.

Any of these factors, many of which are beyond our control, could jeopardize our or our collaboration partners' abilities to obtain regulatory approval for and successfully market roxadustat. Because our business and operations in the near-term are almost entirely dependent upon roxadustat, any significant delays or impediments to regulatory approval could have a material adverse effect on our business and prospects.

In China, the NMPA required that FibroGen Beijing conduct three clinical studies as a post-approval commitment: (i) a post-approval safety study in 2,000 patients; (ii) a drug-intensive monitoring study in 1,000 patients; and (iii) a dosing optimization study in approximately 300 patients on dialysis. Furthermore, in the U.S., we also expect to be required to perform additional clinical trials in order to obtain approval or as a condition to maintaining approval due to post-marketing requirements. If the FDA requires a risk evaluation and mitigation strategy ("REMS"), for any of our product candidates if approved, the substantial cost and expense of complying with a REMS or other post-marketing requirements may limit our ability to successfully commercialize our product candidates.

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Preclinical, Phase 1 and Phase 2 clinical trial results may not be indicative of the results that may be obtained in larger, controlled Phase 3 clinical trials required for approval.*

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical and early clinical trials, which are often highly variable and use small sample sizes, may not be predictive of similar results in humans or in larger, controlled clinical trials, and successful results from early or small clinical trials may not be replicated or show as favorable an outcome, even if successful.

We have conducted a limited number of Phase 2 clinical trials with pamrevlumab. We have conducted a randomized placebo-controlled study in 103 IPF patients with sub-studies in an additional 57 IPF patients comparing pamrevlumab to one of two standards of care, an open-label Phase 2 dose escalation study of pamrevlumab for IPF in 89 patients and a randomized double-blind placebo controlled study for liver fibrosis in subjects with hepatitis B, we are currently conducting an open-label randomized, active-control, neoadjuvant Phase 2 trial in pancreatic cancer combining pamrevlumab with nab-paclitaxel plus gemcitabine in 37 patients, and we are currently in a Phase 2 open-label trial of pamrevlumab for DMD in 21 non-ambulatory patients. We cannot be sure that the results we have received to date from these trials will be substantiated in larger, well-controlled Phase 3 clinical trials, that larger trials will demonstrate the safety and efficacy of pamrevlumab for these or other indications, that further studies will provide benefits over existing approved products or that new safety issues will not be uncovered in further trials. In addition, while we believe that the limited animal and human studies conducted to date suggest that pamrevlumab has the potential to arrest or reverse fibrosis and reduce tumor mass in some patients or diseases, we cannot be sure that these results will be indicative of the effects of pamrevlumab in larger human trials. In addition, the IPF and pancreatic cancer patient populations are extremely ill and routinely experience SAEs, including death, which may be attributed to pamrevlumab in a manner that negatively impacts the safety profile of our product candidate. If the additional clinical trials that we are planning or are currently conducting for pamrevlumab do not show favorable efficacy results or result in safety concerns, or if we do not meet our clinical endpoints with statistical significance, or demonstrate an acceptable risk-benefit profile, we may be prevented from or delay

In the past we developed an earlier generation product candidate aimed at treating anemia in CKD that resulted in a clinical hold for a safety signal seen in that product in Phase 2 clinical trials. The clinical hold applied to that product candidate and roxadustat was lifted for both product candidates after submission of the requested information to the FDA. While we have not seen similar safety concerns involving roxadustat to date, some of the safety concerns associated with the treatment of patients with anemia in CKD using erythropoiesis stimulating agents ("ESAs") did not emerge for many years until placebo-controlled studies had been conducted in large numbers of patients. And while the data monitoring committee for our U.S. and Europe Phase 3 anemia trials has consistently determined that our trials should continue without modification to the protocol, safety issues may still be discovered upon review of unblinded major adverse cardiac event ("MACE") or other data. The biochemical pathways that we believe are affected by roxadustat are implicated in a variety of biological processes and disease conditions, and it is possible that the use of roxadustat to treat larger numbers of patients will demonstrate unanticipated adverse effects, including possible drug interactions, which may negatively impact the safety profile, use and market acceptance of roxadustat. We studied the potential interaction between roxadustat and three statins (atorvastatin, rosuvastatin and simvastatin), which are used to lower levels of lipids in the blood. An adverse effect associated with increased statin plasma concentration is myopathy, which typically presents in a form of myalgia. The studies indicated the potential for increased exposure to those statins when roxadustat is taken simultaneously with those statins and suggested the need for statin dose reductions for patients receiving higher statin doses. We performed additional clinical pharmacology studies to evaluate if the effect of any such interaction could be minimized or eliminated by a modification of the dosing schedule that would separate the administration of roxadustat and the statin by up to 10 hours, however, such studies showed no minimization of effect. It is possible that the potential for interaction between roxadustat and statins could lead to label provisions for statins or roxadustat relating, for example, to dose scheduling or recommended statin dose limitations. In CKD patients, statin therapy is often initiated earlier than treatment for anemia, and risks of myopathy have been shown to decrease with increased time on drug. While we believe the prior statin treatment history of such patients at established doses may reduce the risk of adverse effects from any interaction with roxadustat and facilitate any appropriate dose adjustments, we cannot be sure that this will be the case.

Our Phase 3 trials include a MACE safety endpoint, which is a composite endpoint designed to identify major safety concerns, in particular relating to cardiovascular events such as cardiovascular death, myocardial infarction and stroke. The European Medicines Agency ("EMA") is requiring MACE+ as a safety endpoint which, in addition to the MACE components, incorporates measurements of hospitalization rates due to heart failure or unstable angina. The EMA will also review MACE results. The FDA has also informed us that the MACE endpoint will need to be evaluated separately for our Phase 3 trials in non-dialysis-dependent ("NDD")-CKD patients and our Phase 3 trials in dialysis-dependent ("DD")-CKD patients. The MACE endpoint is being evaluated in pooled analysis across Phase 3 studies of similar study populations and requires demonstration of non-inferiority relative to comparator, which means that the MACE event rate in roxadustat-treated patients must have less than a specified probability of exceeding the rate in the comparator trial by a specified hazard ratio.

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The number of patients necessary in order to permit a statistical analysis with adequate ability to detect the relative risk of MACE or MACE+ events in different arms of the trial, referred to as statistical power, depends on a number of factors, including the rate at which MACE or MACE+ events occur per patient-year in the trial, treatment duration of the patients, the achieved hazard ratios, the rates of discontinuation, and the required statistical power and confidence intervals.

In addition, we cannot be sure that the potential advantages we believe roxadustat may have for treatment of patients with anemia in CKD, as compared to the use of ESAs, will be substantiated by our larger U.S. and European Phase 3 clinical trials, or that we will be able to include a discussion of such advantages in our labeling should we obtain approval. We believe that roxadustat may have certain benefits as compared to ESAs based on the data from our Phase 2 clinical trials and China Phase 3 trials conducted to date, including safety benefits, the absence of a hypertensive effect, the potential to lower cholesterol levels and the potential to correct anemia without the use of IV iron. However, our belief that roxadustat may offer those benefits is based on a limited amount of data from our clinical trials to date, and our understanding of the likely mechanisms of action for roxadustat. Some of these benefits, such as those associated with the apparent effects on blood pressure and cholesterol, are not fully understood and, even if roxadustat receives marketing approval in additional countries beyond China, we do not expect that it will be approved for the treatment of high blood pressure or high cholesterol based on the data from our Phase 3 trials, and we may not be able to refer to any such benefits in the labeling. While the data from our Phase 2 trials suggests roxadustat may reduce low-density lipoprotein ("LDL"), and reduce the ratio of LDL to high-density lipoprotein ("HDL"), the data show it may also reduce HDL, which may be a risk to patients. In addition, causes of the safety concerns associated with the use of ESAs to achieve specified target hemoglobin levels have not been fully elucidated. While we believe that the issues giving rise to these concerns with ESAs are likely due to factors other than the hemoglobin levels achieved, we cannot be certain that roxadustat will not be associated with similar, or more severe, safety concerns.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may face similar setbacks. In addition, the CKD patient population has many afflictions that may cause severe illness or death, which may be attributed to roxadustat in a manner that negatively impacts the safety profile of our product candidate. The results of our completed Phase 3 clinical trials for roxadustat demonstrated efficacy, as all primary efficacy endpoints were met with statistical significance. While we have reported topline cardiovascular safety results, the analysis of these data is ongoing; there may be unanticipated safety concerns or adverse events that prevent from or delay obtaining marketing approval for roxadustat, and even if we obtain marketing approval, any sales of roxadustat may suffer.

We do not know whether our ongoing or planned clinical trials of roxadustat or pamrevlumab will need to be redesigned based on interim results, be able to achieve sufficient enrollment or be completed on schedule, if at all.*

Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- address any physician or patient safety concerns that arise during the course of the trial;
- · obtain required regulatory or institutional review board ("IRB") approval or guidance;
- reach timely agreement on acceptable terms with prospective CROs and clinical trial sites;
- recruit, enroll and retain patients through the completion of the trial;
- maintain clinical sites in compliance with clinical trial protocols;
- initiate or add a sufficient number of clinical trial sites; and
- manufacture sufficient quantities of product candidate for use in clinical trials.

In addition, we could encounter delays if a clinical trial is suspended or terminated by us, by the relevant IRBs at the sites at which such trials are being conducted, or by the FDA or other regulatory authorities. A suspension or termination of clinical trials may result from any number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or a principal investigator's determination that a serious adverse event could be related to our product candidates. Any delays in completing our clinical trials will increase the costs of the trial, delay the product candidate development and approval process and jeopardize our ability to commence marketing and generate revenues. Any of these occurrences may materially and adversely harm our business and operations and prospects.

Our product candidates may cause or have attributed to them undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our product candidates or that may be identified as related to our product candidates by physician investigators conducting our clinical trials or even competing products in development that utilize a similar mechanism of action or act through a similar biological disease pathway could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. Adverse events and SAEs that emerge during treatment with our product candidates or other compounds acting through similar biological pathways may be deemed to be related to our product candidate and may result in:

- our Phase 3 clinical trial development plan becoming longer and more extensive;
- regulatory authorities increasing the data and information required to approve our product candidates and imposing other requirements; and
- our collaboration partners terminating our existing agreements.

The occurrence of any or all of these events may cause the development of our product candidates to be delayed or terminated, which could materially and adversely affect our business and prospects. Refer to "Business - Our Development Program for Roxadustat" and "Business - Pamrevlumab for the Treatment of Fibrosis and Cancer" for a discussion of the adverse events and SAEs that have emerged in clinical trials of roxadustat and pamrevlumab.

Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.

Clinical trials are conducted in representative samples of the potential patient population, which may have significant variability. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, that a more complete safety profile is identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. There have been other products, including ESAs, for which safety concerns have been uncovered following approval by regulatory authorities. Such safety concerns have led to labeling changes or withdrawal of ESAs products from the market. While our most advanced product candidate is chemically unique from ESAs, it or any of our product candidates may be subject to similar risks. For example, roxadustat for use in anemia in CKD is being developed to address a very diverse patient population expected to have many serious health conditions at the time of administration of roxadustat, including diabetes, high blood pressure and declining kidney function.

To date we have not seen evidence of significant safety concerns with our product candidates currently in clinical trials. Patients treated with our products, if approved, may experience adverse reactions and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If safety problems occur or are identified after our product candidates reach the market, we may, or regulatory authorities may require us to amend the labeling of our products, recall our products or even withdraw approval for our products.

We may fail to enroll a sufficient number of patients in our clinical trials in a timely manner, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the rate at which we can recruit and enroll patients in testing our product candidates. Patients may be unwilling to participate in clinical trials of our product candidates for a variety of reasons, some of which may be beyond our control:

- severity of the disease under investigation;
- availability of alternative treatments;
- size and nature of the patient population;
- · eligibility criteria for and design of the study in question;
- perceived risks and benefits of the product candidate under study;
- · ongoing clinical trials of competitive agents;

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- physicians' and patients' perceptions of the potential advantages of our product candidates being studied in relation to available therapies or other products under development;
- our CRO's and our trial sites' efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients and collect patient data adequately during and after treatment.

Patients may be unwilling to participate in our clinical trials for roxadustat due to adverse events observed in other drug treatments of anemia in CKD, and patients currently controlling their disease with existing ESAs may be reluctant to participate in a clinical trial with an investigational drug. We may not be able to successfully initiate or continue clinical trials if we cannot rapidly enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate on-going or planned clinical trials, any of which could have a material and adverse effect on our business and prospects.

If we or third party manufacturers and other service providers on which we rely cannot manufacture sufficient quantities of our product candidates, or at sufficient quality, or perform other services we require, we may experience delays in development, regulatory approval, launch or commercialization.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture and manage our product candidates at sufficient yields and at commercial scale. Although we have entered into commercial supply agreements for the manufacture of some of our raw materials, we have not yet entered into commercial supply agreements with all of our third-party manufacturers. We are continuing to negotiate and expect to enter into commercial supply agreements and other supply management agreements with third-party manufacturers, but we may not be able to enter into these agreements with satisfactory terms or on a timely manner.

We have limited experience manufacturing or managing third parties in manufacturing any of our product candidates in the volumes that are expected to be necessary to support large-scale clinical trials and sales. In addition, we have limited experience forecasting supply requirements or coordinating supply chain (including export management) for launch or commercialization, which is a complex process involving our third-party manufacturers and logistics providers, and for roxadustat, our collaboration partners. We may not be able to accurately forecast supplies for commercial launch, or do so in a timely manner and our efforts to establish these manufacturing and supply chain management capabilities may not meet our requirements as to quantities, scale-up, yield, cost, potency or quality in compliance with cGMP.

We have a limited amount of roxadustat and pamrevlumab in storage, limited capacity reserved at our third-party manufactures, and there are long lead times required to manufacture and scale-up the manufacture of additional supply, as required for both late-stage clinical trials, post-approval trials, and commercial supply. If we are unable to forecast, order or manufacture sufficient quantities of roxadustat or pamrevlumab on a timely basis, it may delay our development, launch or commercialization in some or all indications we are currently pursuing. For example, prior to agreement with regulatory authorities on the scope of our Phase 3 IPF trial design, there is uncertainty as to whether our supply plans will meet our clinical requirements in a timely manner. Any delay or interruption in the supply of our product candidates or products could have a material adverse effect on our business and operations.

Our clinical trials must be conducted with product produced under applicable cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We, and even an experienced third party manufacturer, may encounter difficulties in production. Difficulties may include:

- costs and challenges associated with scale-up and attaining sufficient manufacturing yields, in particular for biologic products such as pamrevlumab, which is a monoclonal antibody;
- supply chain issues, including coordination of multiple contractors in our supply chain and securing necessary licenses (such as export licenses);
- the timely availability and shelf life requirements of raw materials and supplies;
- · quality control and quality assurance;
- shortages of qualified personnel and capital required to manufacture large quantities of product;

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- compliance with regulatory requirements that vary in each country where a product might be sold;
- · capacity or forecasting limitations and scheduling availability in contracted facilities; and
- natural disasters, such as floods, storms, earthquakes, tsunamis, and droughts, or accidents such as fire, that affect facilities, possibly limit or postpone production, and increase costs.

The FDA and EMA will do their own benefit risk analysis and may reach a different conclusion than we or our partners have internally, and these regulatory authorities may base their approval decision on different analyses, data, and statistical methods than ours.*

Even if we believe we have achieved certain results based on a totality of the evidence, such as superiority or non-inferiority, in certain endpoints, populations or subpopulations, or using certain statistical methods of analysis, the FDA and EMA will each conduct their own benefit-risk analysis and may reach different conclusions, using different statistical methods, different endpoints or definitions thereof, or different patient populations or sub-populations, and regulatory authorities may change their approvability criteria based on their internal analyses and discussions with expert advisors. Regulatory authorities may approve roxadustat for fewer or more limited indications than we request, or may grant approval contingent on the performance of costly post-approval clinical trials. While we will present to regulatory authorities certain pre-specified and not pre-specified sub-populations and sub-group analyses (for example, incident dialysis), multiple secondary endpoints, and multiple analytical methods (such as long-term follow up analyses), including adjusted and censored data, regulatory authorities may reject these analyses, methods, or even parts of our trial design or certain data from our studies, the rationale for our pre-specified non-inferiority margins or other portions of our statistical analysis plans. In addition, even if we are able to provide positive data with respect to certain analyses, such as incident dialysis, estimated glomerular filtration rate, hepcidin, or quality of life measures, regulatory authorities may not include such claims on any approved labeling for roxadustat, which may limit the commercialization or market opportunity for roxadustat. Further, initial topline results reported for certain studies (such as reduction of transfusion risk or hemoglobin response in the presence of inflammation), may not be representative of the data seen in all studies or may not be sustained upon further analyses or after more wide-spread use upon commercialization. The failure to obtain regulatory approval, or any label, population or other approval limitations in any jurisdiction, may significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenue.

Positive topline results from our Phase 3 clinical trials assessing the safety and efficacy of roxadustat may not be indicative of additional results or results for roxadustat in other indications.*

There are multiple key and secondary endpoints as well as sub-group analyses in both dialysis and non-dialysis in the U.S. and multiple secondary endpoints in addition to MACE+ as well as sub-group analyses in dialysis and non-dialysis in Europe. We continue to analyze these additional endpoints from the Phase 3 clinical trials of roxadustat in anemia of CKD, as well as from the pooled analyses, some of which may have a bearing on the safety or efficacy of roxadustat. The topline results we have reported thus far may not be indicative of these additional results. In addition, results in these CKD-anemia indications may not be indicative of our clinical trials in other indications or the safety, efficacy, or approvability of roxadustat in other indications.

Even if we are able to obtain regulatory approval of our product candidates, the label we obtain may limit the indicated uses for which our product candidates may be marketed.*

With respect to roxadustat, regulatory approvals, if obtained at all, could limit the approved indicated uses for which roxadustat may be marketed. For example, ESAs have been subject to significant safety warnings, including the "Black Box" warnings on their labels. Refer to "Business - Roxadustat for the Treatment of Anemia in Chronic Kidney Disease - Limitations of the Current Standard of Care for Anemia in CKD" in our annual report on Form 10-K for the year ended December 31, 2018. In addition, in the past, an approved ESA was voluntarily withdrawn due to serious safety issues discovered after approval. The safety concerns relating to ESAs may result in labeling for roxadustat containing similar warnings even if our Phase 3 clinical trials do not suggest that roxadustat has similar safety issues. Even if the label for roxadustat does not contain all of the warnings contained in the "Black Box" warning for ESAs, the label for roxadustat may contain other warnings or limit the market opportunity or approved indications for roxadustat. These warnings could include warnings against exceeding specified hemoglobin targets and other warnings that derive from the lack of clarity regarding the safety issues associated with ESAs, even if our Phase 3 clinical trials do not themselves raise safety concerns.

As an organization, we have not successfully commercialized any drug product. Therefore, we may not be able to efficiently execute our development and commercialization plans.

We are currently conducting Phase 3 clinical trials for pamrevlumab and roxadustat. The conduct of Phase 3 clinical trials and the submission of a successful NDA is a complicated process. As an organization, we have limited experience in preparing, submitting and prosecuting regulatory filings, and have not received approval for an NDA before outside of China where we received marketing authorization in December 2018 from the NMPA for the treatment of anemia caused by CKD in dialysis patients. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to NDA submission and approval of roxadustat or for any other product candidate we are developing, even if our earlier stage clinical trials are successful. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials would prevent us from or delay us in commercializing roxadustat or any other product candidate we are developing.

In addition, in order for any Phase 3 clinical trial to support an NDA submission for approval, the FDA and foreign regulatory authorities require compliance with regulations and standards, including good clinical practices ("GCP") requirements for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to ensure that the data and results from trials are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we as the sponsor remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other regulatory authorities may require us to exclude the use of patient data from our clinical trials not conducted in compliance with GCP or perform additional clinical trials before approving our marketing applications. They may even reject our application for approval or refuse to accept our future applications for an extended time period. For example in China in March 2016, the State Drug Administration, now known as the NMPA issued guidance related to its clinical trial data integrity regulations. While trial sites and CROs bear liability for the accuracy and authenticity of data they are directly responsible for, the sponsor ultimately bears full responsibility for submitted clinical data and the drug application dossier. Fraudulent clinical data could result in a ban in China of a sponsor's product-related NDA applications for three years and other NDA applications for one year. We have taken extensive steps to ensure the integrity of our China clinical data. In China, the clinical site inspections confirmed our compliance with GCP regulations and supported our approval. However, we cannot assure you that upon inspection by a regulatory authority in other regions, such regulatory authority will determine that any of our clinical trials comply with GCP requirements or that our results will be deemed authentic or may be used in support of our regulatory submissions.

If we are unable to establish sales, marketing and distribution capabilities or enter into or maintain agreements with third parties to market and sell our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sales, marketing or distribution of pharmaceutical products in any country. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales and marketing capabilities or make and maintain our existing arrangements with third parties to perform these services at a level sufficient to support our commercialization efforts.

To the extent that we would undertake sales and marketing of any of our products directly, there are risks involved with establishing our own sales, marketing and distribution capabilities. Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to effectively manage geographically dispersed sales and marketing teams;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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With respect to roxadustat, we are dependent on the commercialization capabilities of our collaboration partners, AstraZeneca and Astellas. If either such partner were to terminate its agreement with us, we would have to commercialize on our own or with another third party. We will have limited or little control over the commercialization efforts of such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products, if any, effectively. If they are not successful in commercializing our product candidates, our business and financial condition would suffer.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.*

The development and commercialization of new pharmaceutical products is highly competitive. Our future success depends on our ability to achieve and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to discover, develop and commercialize new products with superior efficacy, convenience, tolerability, and safety. We expect that in many cases, the products that we commercialize will compete with existing, market-leading products of companies that have large, established commercial organizations.

If roxadustat is approved and launched commercially, competing drugs are expected to include ESAs, particularly in those patient segments where ESAs are used. Currently available ESAs include epoetin alfa (EPOGEN ®, marketed by Amgen Inc. in the U.S., Procrit ® and Erypo ®/Eprex ®, marketed by Johnson & Johnson Inc., and Espo ® marketed by Kyowa Hakko Kirin in Japan and China), darbepoetin (Amgen/Kyowa Hakko Kirin's Aranesp ® and NESP ®) and Mircera ® marketed by Hoffmann-La Roche ("Roche") outside of the U.S. and by Vifor Pharma ("Vifor"), a Roche licensee, in the U.S. and Puerto Rico, as well as biosimilar versions of these currently marketed ESA products. ESAs have been used in the treatment of anemia in CKD for more than 20 years, serving a significant majority of DD-CKD patients. While NDD-CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated, some patients under nephrology care may be receiving ESA therapy. It may be difficult to encourage healthcare providers and patients to switch to roxadustat from products with which they have become familiar.

We may also face competition from potential new anemia therapies currently in clinical development, including in those patient segments not currently addressed by ESAs. Companies such as GlaxoSmithKline plc ("GSK"), Bayer Corporation ("Bayer"), Akebia Therapeutics, Inc. ("Akebia"), and Japan Tobacco, are currently developing HIF prolyl hydroxylase ("HIF-PH") inhibitors for anemia in CKD indications. Akebia is currently conducting Phase 3 studies in NDD-CKD and DD-CKD, as well as additional Phase 1 and Phase 2 studies. In Japan, Mitsubishi Tanabe Pharmaceutical Corporation ("Mitsubishi Tanabe"), Akebia's collaboration partner, submitted an NDA for treatment of anemia in CKD patients on dialysis and not on dialysis, supported by the Phase 3 studies conducted by Mitsubishi Tanabe in Japan. GSK is conducting global Phase 3 studies in NDD-CKD and DD-CKD. In Japan, GSK has completed two Phase 3 studies in hemodialysis-dependent CKD patients and one Phase 3 study in CKD patients not on dialysis or on peritoneal dialysis. GSK and Kyowa Hakko Kirin announced in November 2018 that the two companies signed a strategic commercialization deal in Japan for daprodustat. Bayer has completed global Phase 2 studies and announced in May 2017 its HIF-PH inhibitor is now in continued development in Japan only, and its Japan Phase 3 studies in NDD-CKD and DD-CKD are expected to complete in the second half of 2019. Japan Tobacco is also conducting Phase 3 studies in NDD-CKD and DD-CKD in Japan only. Some of these product candidates may enter the market prior to roxadustat.

In addition, there are other companies developing biologic therapies for the treatment of other anemia indications that we may also seek to pursue in the future, including anemia of MDS. For example, Acceleron Pharma Inc. and its partner Celgene Corporation ("Celgene") announced in April 2019 that Celgene has submitted a Biologics License Application ("BLA") for luspatercept for the treatment of adult patients with very low to intermediate risk of MDS-associated anemia who have ring sideroblasts and require red blood cell transfusions, and beta-thalassemia-associated anemia who require red blood cell transfusions. Celgene's plan to submit a marketing approval application for luspatercept in the European Union ("EU") in the second quarter of 2019. There may also be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat if and when it is commercialized.

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In China, biosimilars of epoetin alfa are offered by Chinese pharmaceutical companies such as EPIAO marketed by 3SBio Inc. as well as more than 15 other local manufacturers. We may also face competition by HIF-PH inhibitors from other companies such as Akebia, Bayer, and GSK, which was authorized by the NMPA to conduct trials in China to support its ex-China regulatory filings. Furthermore, while it is too early to understand how the NMPA will implement its recently approved guidelines to allow multinational companies to use their ex-China clinical data in their NDAs in China, these guidelines could in theory allow competitors to accelerate their NDA applications in China. Akebia announced in December 2015 that it has entered into a development and commercialization partnership with Mitsubishi Tanabe for its HIF-PH inhibitor vadadustat in Japan, Taiwan, South Korea, India, and certain other countries in Asia, and announced in April 2017 an expansion of their U.S. collaboration with Otsuka to add markets, including China. 3SBio Inc. also announced in 2016 its plan to begin a Phase 1 clinical trial of a HIF-PH inhibitor for the China market, and two Chinese domestic companies, Jiangsu Hengrui Medicine Co., Ltd. and Guangdong Sunshine Health Investment Co., Ltd., have announced they also secured the NMPA approval to conduct clinical trials for their respective HIF-PH inhibitors.

The first biosimilar ESAs, Pfizer's Retacrit® (epoetin zeta), entered the U.S. market in November 2018. Market penetration of Retacrit® (epoetin zeta) and the potential addition of other biosimilar ESAs, currently under development, may alter the competitive and pricing landscape of anemia therapy in DD-CKD patients under the end stage renal disease bundle. The patents for Amgen's epoetin alfa, EPOGEN, expired in 2004 in the EU, and the final material patents in the U.S. expired in May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in the EU, China and other territories. In the U.S., a few ESA biosimilars are currently under development. Sandoz, a division of Novartis, markets Binocrit ® (epoetin alfa) in Europe and may file a biosimilar BLA in the U.S.

The majority of the current CKD anemia market focuses on dialysis patients, who visit dialysis centers on a regular basis, typically three-times a week, and anemia therapies are administered as part of the visit. Two of the largest operators of dialysis clinics in the U.S., DaVita Healthcare Partners Inc. ("DaVita") and Fresenius Medical Care AG & Co. KGaA ("Fresenius"), collectively provide dialysis care to approximately 70% of U.S. dialysis patients, and therefore have historically won long-term contracts including rebate terms with Amgen. In January 2017, DaVita entered into a new 6-year sourcing and supply agreement with Amgen that is effective through 2022. Fresenius' contract with Amgen expired in 2015, and Fresenius is now administering Mircera® in a significant portion of its U.S. dialysis patients since Mircera was made available by Vifor. Successful penetration of this market may require a significant agreement with Fresenius or DaVita on favorable terms and on a timely basis.

If pamrevlumab is approved and launched commercially to treat IPF, competing drugs are expected to include Roche's Esbriet® (pirfenidone) and Boehringer Ingelheim Pharma GmbH & Co. KG's Ofev® (nintedanib). Nintedanib is also in development for non-small cell lung cancer and ovarian cancer. Other potential competitive product candidates in development for IPF include Biogen-Idec's BG-00011, Galapagos NV's GLPG1690 and GLPG1205, Kadmon Holdings, Inc.'s KD025, Prometic Life Sciences Inc.'s PBI-4050, and Promedior Inc.'s PRM-151. Galapagos initiated a Phase 3 study for GLPG 1690 in December 2018.

If pamrevlumab is approved and launched commercially to treat locally advanced pancreatic cancer patients who are not candidates for surgical resection, pamrevlumab may face competition from agents seeking approval in combination with gemcitibine and nab-paclitaxel from companies such as NewLink Genetics Corporation and Halozyme Therapeutics, Inc. Gemcitabine and/or nab-paclitaxel are the current standard of care in the first-line treatment of metastatic pancreatic cancer. Celgene Corporation's Abraxane® (nab-paclitaxel) was launched in the U.S. and Europe in 2013 and 2014, and was the first drug approved in this disease in nearly a decade.

If pamrevlumab is approved and launched commercially to treat DMD, pamrevlumab may face competition for some patients from Sarepta Therapeutics, Inc. ("Sarepta") with Exondys 51® (eteplirsen), approved in the U.S. for patients who have a confirmed mutation in the DMD gene that is amenable to exon 51 skipping, and from PTC Therapeutics' drug ataluren approved in ambulatory patients in Europe. We may also face competition from Sarepta's golodirsen, currently under NDA review in the U.S., and agents currently in development for DMD, including PTC Therapeutics' ataluren, Santhera Pharmaceuticals' idebone, Catabasis Pharmaceuticals' edasalonexent, Capricor Therapeutics' CAP-1002, and Sarepta's casimersen and other gene therapies, if and when these agents are approved and launched.

The success of any or all of these potential competitive products may negatively impact the development and potential for success of pamrevlumab. In addition, any competitive products that are on the market or in development may compete with pamrevlumab for patient recruitment and enrollment for clinical trials or may force us to change our clinical trial design, including, in order to compare pamrevlumab against another drug, which may be the new standard of care.

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If FG-5200 is approved and launched in China to treat corneal blindness resulting from partial thickness corneal damage without active inflammation and infection, it is likely to compete with other products designed to treat corneal damage. For example, in April 2015, a subsidiary of China Regenerative Medicine International Limited received approval for their acellular porcine cornea stroma medical device to treat patients in China with corneal ulcers and in April 2016, Guangzhou Yourvision Biotech Co. Ltd, a subsidiary of Guanhao Biotech, received approval for their acellular porcine cornea medical device to treat patients in China with infectious keratitis that does not respond to drug treatment.

Moreover, many of our competitors have significantly greater resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients, manufacturing pharmaceutical products, and commercialization. In the potential anemia market for roxadustat, for example, large and established companies such as Amgen and Roche, among others, compete aggressively to maintain their market shares. In particular, the currently marketed ESA products are supported by large pharmaceutical companies that have greater experience and expertise in commercialization in the anemia market, including in securing reimbursement, government contracts and relationships with key opinion leaders; conducting testing and clinical trials; obtaining and maintaining regulatory approvals and distribution relationships to market products; and marketing approved products. These companies also have significantly greater scale research and marketing capabilities than we do and may also have products that have been approved or are in later stages of development, and have collaboration agreements in our target markets with leading dialysis companies and research institutions. These competitors have in the past successfully prevented new and competing products from entering the anemia market, and we expect that their resources will represent challenges for us and our collaboration partners, AstraZeneca and Astellas. If we and our collaboration partners are not able to compete effectively against existing and potential competitors, our business and financial condition may be materially and adversely affected.

Our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third party payors and others in the health care community.

Even if we obtain marketing approval for roxadustat, pamrevlumab or any other product candidates that we may develop or acquire in the future in all indications and geographic regions, these product candidates may not gain market acceptance among physicians, third party payors, patients and others in the health care community. Market acceptance of any approved product, including in roxadustat for the treatment of anemia caused by CKD in dialysis patients in China, depends on a number of other factors, including:

- the clinical indications for which the product is approved and the labeling required by regulatory authorities for use with the product, including any warnings that may be required in the labeling;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety, efficacy and convenience of treatment in relation to alternative treatments;
- the restrictions on the use of our products together with other medications, if any;
- the availability of adequate coverage and reimbursement or pricing by third party payors and government authorities;
- the ability of treatment providers, such as dialysis clinics, to enter into relationships with us without violating their existing agreement;
- the effectiveness of our sales and marketing efforts.

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No or limited reimbursement or insurance coverage of our approved products, if any, by third party payors may render our products less attractive to patients and healthcare providers.

Market acceptance and sales of any approved products will depend significantly on reimbursement or coverage of our products by the Chinese government or third party payors, and may be affected by existing and future healthcare reform measures or prices of related products for which the government or third party reimbursement applies. Coverage and reimbursement by the government or a third party payor may depend upon a number of factors, including the payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

The review and publication cycle for the Chinese government to update their reimbursement lists (national or provincial) is unpredictable and is outside our control.

Obtaining coverage and reimbursement approval for a product from a government or other third party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor, which we may not be able to provide. Furthermore, the reimbursement policies of third party payors may significantly change in a manner that renders our clinical data insufficient for adequate reimbursement or otherwise limits the successful marketing of our products. Even if we obtain coverage for our product candidates, third party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products.

Price controls may limit the price at which products such as roxadustat, if approved, are sold. For example, reference pricing is used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partner may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unacceptable levels, we or our partner may elect not to commercialize our products in such countries, and our business and financial condition could be adversely affected.

Risks Related to Our Reliance on Third Parties

If our collaborations with Astellas or AstraZeneca were terminated, or if Astellas or AstraZeneca were to prioritize other initiatives over their collaborations with us, whether as a result of a change of control or otherwise, our ability to successfully develop and commercialize our lead product candidate, roxadustat, would suffer.

We have entered into collaboration agreements with respect to the development and commercialization of our lead product candidate, roxadustat, with Astellas and AstraZeneca. These agreements provide for reimbursement of our development costs by our collaboration partners and also provide for commercialization of roxadustat throughout the major territories of the world.

Our agreements with Astellas and AstraZeneca provide each of them with the right to terminate their respective agreements with us, upon the occurrence of negative clinical results, delays in the development and commercialization of our product candidates or adverse regulatory requirements or guidance. The termination of any of our collaboration agreements would require us to fund and perform the further development and commercialization of roxadustat in the affected territory, or pursue another collaboration, which we may be unable to do, either of which could have an adverse effect on our business and operations. In addition, each of those agreements provides our respective partners the right to terminate any of those agreements upon written notice for convenience. Moreover, if Astellas or AstraZeneca, or any successor entity, were to determine that their collaborations with us are no longer a strategic priority, or if either of them or a successor were to reduce their level of commitment to their collaborations with us, our ability to develop and commercialize roxadustat could suffer. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaboration agreements with other parties in the area or field of exclusivity.

If we fail to establish and maintain strategic collaborations related to our product candidates, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise at significant cost. This in turn may negatively affect the development of our other product candidates as we direct resources to our most advanced product candidates.

Conflicts with our collaboration partners could jeopardize our collaboration agreements and our ability to commercialize product candidates.

Our collaboration partners have certain rights to control decisions regarding the development and commercialization of our product candidates with respect to which they are providing funding. If we have a disagreement over strategy and activities, our plans for obtaining approval may be revised and negatively affect the anticipated timing and potential for success of our product candidates. Even if a product under a collaboration agreement is approved, we will remain substantially dependent on the commercialization strategy and efforts of our collaboration partners, and neither of our collaboration partners has experience in commercialization of a novel drug such as roxadustat in the dialysis market.

With respect to our collaboration agreements for roxadustat, there are additional complexities in that we and our collaboration partners, Astellas and AstraZeneca, must reach consensus on our Phase 3 development program. Multi-party decision-making is complex and involves significant time and effort, and there can be no assurance that the parties will cooperate or reach consensus, or that one or both of our partners will not ask to proceed independently in some or all of their respective territories or functional areas of responsibility in which the applicable collaboration partner would otherwise be obligated to cooperate with us. Any disputes or lack of cooperation with us by either Astellas or AstraZeneca may negatively impact the timing or success of our planned Phase 3 clinical studies.

We intend to conduct proprietary research programs in specific disease areas that are not covered by our collaboration agreements. Our pursuit of such opportunities could, however, result in conflicts with our collaboration partners in the event that any of our collaboration partners takes the position that our internal activities overlap with those areas that are exclusive to our collaboration agreements, and we should be precluded from such internal activities. Moreover, disagreements with our collaboration partners could develop over rights to our intellectual property. In addition, our collaboration agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaboration partners could lead to the termination of our collaboration agreements, delay collaborative activities, reduce our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaboration partners.

Certain of our collaboration partners could also become our competitors in the future. If our collaboration partners develop competing products, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our product candidates, the development and commercialization of our product candidates and products could be delayed.

We rely on third parties for the conduct of most of our preclinical and clinical trials for our product candidates, and if our third party contractors do not properly and successfully perform their obligations under our agreements with them, we may not be able to obtain or may be delayed in receiving regulatory approvals for our product candidates.

We rely heavily on university, hospital, dialysis centers and other institutions and third parties, including the principal investigators and their staff, to carry out our clinical trials in accordance with our clinical protocols and designs. We also rely on a number of third party CROs to assist in undertaking, managing, monitoring and executing our ongoing clinical trials, including those for roxadustat. We expect to continue to rely on CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our development efforts in the future, including our Phase 3 development program for roxadustat. We compete with many other companies for the resources of these third parties, and large pharmaceutical companies often have significantly more extensive agreements and relationships with such third party providers, and such third party providers may prioritize the requirements of such large pharmaceutical companies over ours. The third parties on whom we rely may terminate their engagements with us at any time, which may cause delay in the development and commercialization of our product candidates. If any such third party terminates its engagement with us or fails to perform as agreed, we may be required to enter into alternative arrangements, which would result in significant cost and delay to our product development program. Moreover, our agreements with such third parties generally do not provide assurances regarding employee turnover and availability, which may cause interruptions in the research on our product candidates by such third parties.

Moreover, while our reliance on these third parties for certain development and management activities will reduce our control over these activities, it will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP requirements for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results from trials are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we, as the sponsor, remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites.

If any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, other regulations, trial protocol or other requirements under their agreements with us, the quality or accuracy of the data they obtain may be compromised or unreliable, and the trials of our product candidates may not meet regulatory requirements. If trials do not meet regulatory requirements or if these third parties need to be replaced, the development of our product candidates may be delayed, suspended or terminated, regulatory authorities may require us to exclude the use of patient data from our approval applications or perform additional clinical trials before approving our marketing applications. Regulatory authorities may even reject our application for approval or refuse to accept our future applications for an extended time period. We cannot assure that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements or that our results may be used in support of our regulatory submissions. If any of these events occur, we may not be able to obtain regulatory approval for our product candidates on a timely basis, at a reasonable cost, or at all.

We currently rely, and expect to continue to rely, on third parties to conduct many aspects of our clinical studies and product manufacturing, and these third parties may not perform satisfactorily.

We do not have operating manufacturing facilities at this time other than our roxadustat and FG-5200 manufacturing facility in China, and our current commercial manufacturing facility plans in China are not expected to satisfy the requirements necessary to support development and commercialization outside of China. Other than in and for China specifically, we do not expect to independently manufacture our products. We currently rely, and expect to continue to rely, on third parties to scale-up, manufacture and supply roxadustat and our other product candidates outside of China. Risks arising from our reliance on third party manufacturers include:

- reduced control and additional burdens of oversight as a result of using third party manufacturers for all aspects of manufacturing activities, including regulatory compliance and quality control and quality assurance;
- termination of manufacturing agreements, termination fees associated with such termination, or nonrenewal of manufacturing
 agreements with third parties may negatively impact our planned development and commercialization activities;
- the possible misappropriation of our proprietary technology, including our trade secrets and know-how; and
- disruptions to the operations of our third party manufacturers or suppliers unrelated to our product, including the merger, acquisition, or bankruptcy of a manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers.

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Any of these events could lead to development delays or failure to obtain regulatory approval, or affect our ability to successfully commercialize our product candidates. Some of these events could be the basis for action by the FDA or another regulatory authority, including injunction, recall, seizure or total or partial suspension of production.

The facilities used by our contract manufacturer to manufacture our product candidates must pass inspections by the FDA and other regulatory authorities. Although, except for China, we do not control the manufacturing operations of, and expect to remain completely dependent on, our contract manufacturers for manufacture of drug substance and finished drug product, we are ultimately responsible for ensuring that our product candidates are manufactured in compliance with cGMP requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our or our collaboration partners' specifications, or the regulatory requirements of the FDA or other regulatory authorities, we may not be able to secure and/or maintain regulatory approval for our product candidates and our development or commercialization plans may be delayed. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. In addition, although our longer-term agreements are expected to provide for requirements to meet our quantity and quality requirements to manufacture our products candidates for clinical studies and commercial sale, we will have minimal direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel and we expect to rely on our audit rights to ensure that those qualifications are maintained to meet our requirements. If our contract manufacturers' facilities do not pass inspection by regulatory authorities, or if regulatory authorities do not approve these facilities for the manufacture of our products, or withdraw any such approval in the future, we would need to identify and qualify alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products, if approved. Moreover, any failure of our third party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or adverse regulatory consequences, including clinical holds, warnings or untitled letters, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which would be expected to significantly and adversely affect supplies of our products to us and our collaboration partners.

Any of our third party manufacturers may terminate their engagement with us at any time and we have not yet entered into any commercial supply agreements for the manufacture of active pharmaceutical ingredients ("APIs") or drug products. With respect to roxadustat, AstraZeneca and Astellas have certain rights to assume manufacturing of roxadustat and the existence of those rights may limit our ability to enter into favorable long-term supply agreements, if at all, with other third party manufacturers. In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access and prioritization to manufacture. Certain third party manufacturers may be contractually prohibited from manufacturing our product due to non-compete agreements with our competitors or a commitment to grant another party priority relative to our products. There are a limited number of third party manufacturers that operate under cGMP and that might be capable of manufacturing to meet our requirements. Due to the limited number of third party manufacturers with the contractual freedom, expertise, required regulatory approvals and facilities to manufacture our products on a commercial scale, identifying and qualifying a replacement third party manufacturer would be expensive and time-consuming and may cause delay or interruptions in the production of our product candidates or products, which in turn may delay, prevent or impair our development and commercialization efforts.

We have a letter agreement with IRIX Pharmaceuticals, Inc. ("IRIX"), a third party manufacturer that we have used in the past, pursuant to which we agreed to negotiate a single source manufacturing agreement that included a right of first negotiation for the cGMP manufacture of HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third party bids within 5%. The exclusive right to manufacture extends for five years after approval of an NDA for those compounds, and any agreement would provide that no minimum amounts would be specified until appropriate by forecast and that we and a commercialization partner would have the rights to contract with independent third parties that exceed IRIX's internal manufacturing capabilities or in the event that we or our commercialization partner determines for reasons of continuity of supply and security that such a need exists, provided that IRIX would supply no less than 65% of the product if it is able to provide this level of supply. Subsequent to the letter agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the letter agreement with respect to the single source manufacturing agreement, and if we were to enter into any such exclusive manufacturing agreement, there can be no assurance that IRIX will not assert a claim for right to manufacture roxadustat or that IRIX could manufacture roxadustat successfully and in accordance with applicable regulations for a commercial product and the specifications of our collaboration partners. In 2015, Patheon Pharmaceuticals Inc., a business unit of DPx Holdings B.V. ("Patheon"), acquired IRIX, and in 2017 ThermoFisher Scientific Inc. acquired Patheon.

If any third party manufacturer terminates its engagement with us or fails to perform as agreed, we may be required to find replacement manufacturers, which would result in significant cost and delay to our development programs. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such third party or potential second source manufacturer. In any event, with any third party manufacturer we expect to enter into technical transfer agreements and share our know-how with the third party manufacturer, which can be time-consuming and may result in delays. These delays could result in a suspension or delay of marketing roxadustat.

Certain of the components of our product candidates are acquired from single-source suppliers and have been purchased without long-term supply agreements. The loss of any of these suppliers, or their failure to supply us with supplies of sufficient quantity and quality to complete our drug substance or finished drug product of acceptable quality and an acceptable price, would materially and adversely affect our business.

We do not have an alternative supplier of certain components of our product candidates. To date, we have used purchase orders for the supply of materials that we use in our product candidates. We may be unable to enter into long-term commercial supply arrangements with our vendors, or do so on commercially reasonable terms, which could have a material adverse impact upon our business. In addition, we currently rely on our contract manufacturers to purchase from third-party suppliers some of the materials necessary to produce our product candidates. We do not have direct control over the acquisition of those materials by our contract manufacturers. Moreover, we currently do not have any agreements for the commercial production of those materials.

The logistics of our supply chain, which include shipment of materials and intermediates from countries such as China and India add additional time and risk (including risk of loss) to the manufacture of our product candidates. While we have in the past maintained sufficient inventory of materials, API, and drug product to meet our and our collaboration partners' needs for roxadustat to date, the lead time and regulatory approvals required to source from and into countries outside of the U.S. increase the risk of delay and potential shortages of supply.

Risks Related to Our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and contractual arrangements to protect the intellectual property related to our technologies. We will only be able to protect our products and proprietary information and technology by preventing unauthorized use by third parties to the extent that our patents, trade secrets, and contractual position allow us to do so. Any disclosure to or misappropriation by third parties of our trade secrets or confidential information could compromise our competitive position. Moreover, we are involved in, have in the past been involved in, and may in the future be involved in legal or administrative proceedings involving our intellectual property initiated by third parties, and which proceedings can result in significant costs and commitment of management time and attention. As our product candidates continue in development, third parties may attempt to challenge the validity and enforceability of our patents and proprietary information and technologies.

We also are involved in, have in the past been involved in, and may in the future be involved in initiating legal or administrative proceedings involving the product candidates and intellectual property of our competitors. These proceedings can result in significant costs and commitment of management time and attention, and there can be no assurance that our efforts would be successful in preventing or limiting the ability of our competitors to market competing products.

Composition-of-matter patents relating to the API are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection not limited to any one method of use. Method-of-use patents protect the use of a product for the specified method(s), and do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. We rely on a combination of these and other types of patents to protect our product candidates, and there can be no assurance that our intellectual property will create and sustain the competitive position of our product candidates.

Biotechnology and pharmaceutical product patents involve highly complex legal and scientific questions and can be uncertain. Any patent applications that we own or license may fail to result in issued patents. Even if patents do successfully issue from our applications, third parties may challenge their validity or enforceability, which may result in such patents being narrowed, invalidated, or held unenforceable. Even if our patents and patent applications are not challenged by third parties, those patents and patent applications may not prevent others from designing around our claims and may not otherwise adequately protect our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, competitors with significantly greater resources could threaten our ability to commercialize our product candidates. Discoveries are generally published in the scientific literature well after their actual development, and patent applications in the U.S. and other countries are typically not published until 18 months after their filing, and in some cases are never published. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or patent applications, or that we or our licensors were the first to file for patent protection covering such inventions. Subject to meeting other requirements for patentability, for U.S. patent applications filed prior to March 16, 2013, the first to invent the claimed invention is entitled to receive patent protection for that invention while, outside the U.S., the first to file a patent application encompassing the invention is entitled to patent protection for the invention. The U.S. moved to a "first to file" system under the Leahy-Smith America Invents Act ("AIA"), effective March 16, 2013. This system also includes procedures for challenging issued patents and pending patent applications, which creates additional uncertainty. We may become involved in opposition or interference proceedings challenging our patents and patent applications or the patents and patent applications of others, and the outcome of any such proceedings are highly uncertain. An unfavorable outcome in any such proceedings could reduce the scope of or invalidate our patent rights, allow third parties to commercialize our technology and compete directly with us, or result in our inability to manufacture, develop or commercialize our product candidates without infringing the patent rights of others.

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In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to assign their inventions to us, and we require all of our employees, consultants, advisors and any third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how and other information and technology. Furthermore, the laws of some foreign countries, in particular, China, where we have operations, do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business and operations.

Intellectual property disputes with third parties and competitors may be costly and time consuming, and may negatively affect our competitive position.*

Our commercial success may depend on our avoiding infringement of the patents and other proprietary rights of third parties as well as on enforcing our patents and other proprietary rights against third parties. Pharmaceutical and biotechnology intellectual property disputes are characterized by complex, lengthy and expensive litigation over patents and other intellectual property rights. We may initiate or become party to or be threatened with future litigation or other proceedings regarding intellectual property rights with respect to our product candidates and competing products.

As our product candidates progress toward commercialization, we or our collaboration partners may be subject to patent infringement claims from third parties. We attempt to ensure that our product candidates do not infringe third party patents and other proprietary rights. However, the patent landscape in competitive product areas is highly complex, and there may be patents of third parties of which we are unaware that may result in claims of infringement. Accordingly, there can be no assurance that our product candidates do not infringe proprietary rights of third parties, and parties making claims against us may seek and obtain injunctive or other equitable relief, which could potentially block further efforts to develop and commercialize our product candidates including roxadustat or pamrevlumab. Any litigation involving defense against claims of infringement, regardless of the merit of such claims, would involve substantial litigation expense and would be a substantial diversion of management time.

We may consider administrative proceedings and other means for challenging third party patents and patent applications. An unfavorable outcome in any such challenge could require us to cease using the related technology and to attempt to license rights to it from the prevailing third party, which may not be available on commercially reasonable terms, if at all, in which case our business could be harmed.

We intend, if necessary, to vigorously enforce our intellectual property in order to protect the proprietary position of our product candidates, including roxadustat and pamrevlumab. In addition, our collaboration partners who have been granted licenses to our patents may also have rights related to enforcement of those patents. Active efforts to enforce our patents by us or by our partners may include litigation, administrative proceedings, or both, depending on the potential benefits that might be available from those actions and the costs associated with undertaking those efforts against third parties. We carefully review and monitor publicly available information regarding products that may be competitive with our product candidates and assert our intellectual property rights where appropriate. For example, we previously prevailed in an administrative challenge initiated by a major biopharmaceutical company regarding our intellectual property rights, maintaining our intellectual property in all relevant scope, and will continue to protect and enforce our intellectual property rights. In addition, our partner Astellas has recently initiated *quia timet* infringement actions against Akebia and GSK based on our specific patents in the United Kingdom in response to actions taken by Akebia and GSK against those patents, as further detailed below.

Third parties may also challenge our patents and patent applications, through interference, reexamination, *inter partes* review, and post-grant review proceedings before the U.S. Patent and Trademark Office ("USPTO") or through comparable proceedings in other territories. For example, Akebia and others have filed oppositions against certain European patents within our HIF anemia-related technologies patent portfolio. In three of these proceedings, for FibroGen European Patent Nos. 1463823, 1633333, and 2322155, the European Patent Office has handed down decisions unfavorable to FibroGen. In a fourth of these proceedings, the European Patent Office issued a decision favorable to FibroGen, maintaining FibroGen European Patent No. 2322153 in amended form. All of these decisions are currently under appeal, and these four patents are valid and enforceable pending resolution of the appeals. The ultimate outcomes of such proceedings remain uncertain, and ultimate resolution of the appeals may take two years or longer. In addition, Akebia recently filed oppositions against FibroGen European Patent Nos. 2289531 and 2298301. As mentioned above, Akebia and GSK have also initiated actions in the United Kingdom against the United Kingdom counterparts of each of these European Patent Nos. 2322153 and 2322155) with respect to its daprodustat product. Akebia is also pursuing invalidation actions against corresponding patents in Canada and in Japan. While we believe the ultimate outcome of all proceedings will be that these FibroGen patents will be upheld in relevant part, we note that narrowing or even revocation of any of these patents would not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia.

Oppositions have also recently been filed against our European Patent No. 2872488, which claims a crystalline form of roxadustat.

Furthermore, there is a risk that any public announcements concerning the status or outcomes of intellectual property litigation or administrative proceedings may adversely affect the price of our stock. If securities analysts or our investors interpret such status or outcomes as negative or otherwise creating uncertainty, our common stock price may be adversely affected.

Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.

Our reliance on third party contractors to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our trade secrets and know-how. Despite the contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations in place with our collaboration partners. Despite our efforts to protect our trade secrets and other confidential information, a competitor's discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

We have an extensive worldwide patent portfolio. The cost of maintaining our patent protection is high and maintaining our patent protection requires continuous review and compliance in order to maintain worldwide patent protection. We may not be able to effectively maintain our intellectual property position throughout the major markets of the world.

The USPTO and foreign patent authorities require maintenance fees and payments as well as continued compliance with a number of procedural and documentary requirements. Noncompliance may result in abandonment or lapse of the subject patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance may result in reduced royalty payments for lack of patent coverage in a particular jurisdiction from our collaboration partners or may result in competition, either of which could have a material adverse effect on our business.

We have made, and will continue to make, certain strategic decisions in balancing costs and the potential protection afforded by the patent laws of certain countries. As a result, we may not be able to prevent third parties from practicing our inventions in all countries throughout the world, or from selling or importing products made using our inventions in and into the U.S. or other countries. Third parties may use our technologies in territories in which we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories which provide inadequate enforcement mechanisms, even if we have patent protection. Such third party products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the U.S., and we may encounter significant problems in securing and defending our intellectual property rights outside the U.S.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries such as China, do not always favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop infringement of our patents, misappropriation of our trade secrets, or marketing of competing products in violation of our proprietary rights. In China, our intended establishment of significant operations will depend in substantial part on our ability to effectively enforce our intellectual property rights in that country. Proceedings to enforce our intellectual property rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, and could put our patents in these territories at risk of being invalidated or interpreted narrowly, or our patent applications at risk of not being granted, and could provoke third parties to assert claims against us. We may not prevail in all legal or other proceedings that we may initiate and, if we were to prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Intellectual property rights do not address all potential threats to any competitive advantage we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and intellectual property rights may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not
 covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- The prosecution of our pending patent applications may not result in granted patents.
- Granted patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid
 or unenforceable, as a result of legal challenges by our competitors.
- Patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product.
- Our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from
 patent infringement claims for such activities, as well as in countries in which we do not have patent rights, and may then use the
 information learned from such activities to develop competitive products for sale in markets where we intend to market our product
 candidates.

Roxadustat is considered a Class 2 substance on the 2019 World Anti-Doping Agency Prohibited List which could limit sales and increase security and distribution costs for us and our partners, particularly in China.

Roxadustat is considered a Class 2 substance on the World Anti-Doping Agency ("WADA") Prohibited List. There are enhanced security and distribution procedures we and our collaboration partners and third-party contractors will have to take to limit the risk of loss of product in the supply chain. As a result, our distribution, manufacturing and sales costs for roxadustat, as well as for our partners, will be increased which will reduce profitability. In addition there is a risk of reduced sales due to patient access to this drug. This is particularly the case in China where we will not be able to sell roxadustat in private pharmacies due to the WADA classification. While private pharmacies only represent approximately 10% of the market in China, this will negatively affect sales and therefore the profitability of roxadustat and the Company as a whole.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold or used for research under the same or similar names, or similar mechanism of action or product class, but which are sold without proper licenses or approvals, and are often lower cost, lower quality, different potency, or have different ingredients or formulations, and have the potential to damage the reputation for quality and effectiveness of the genuine product. Such products may be used for indications or purposes that are not recommended or approved or for which there is no data or inadequate data with regard to safety or efficacy. Such products divert sales from genuine products. If counterfeit pharmaceuticals illegally sold or used for research result in adverse events or side effects to consumers, we may be associated with any negative publicity resulting from such incidents. Consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. In addition, the use of counterfeit products could be used in non-clinical or clinical studies, or could otherwise produce undesirable side effects or adverse events that may be attributed to our products as well, which could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for the commercialization of our product candidates.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. Except in China, We have not obtained regulatory approval for any product candidate, and it is possible that neither roxadustat nor pamrevlumab, nor any future product candidates we may discover, in-license or acquire and seek to develop in the future, will obtain regulatory approval in countries other than China.

Our product candidates could fail to receive regulatory approval from the FDA or other regulatory authorities for many reasons, including:

- disagreement over the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement over our interpretation of data from preclinical studies or clinical trials;
- disagreement over whether to accept efficacy results from clinical trial sites outside the U.S. where the standard of care is potentially different from that in the U.S.:
- the insufficiency of data collected from clinical trials of our present or future product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;

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- disapproval of the manufacturing processes or facilities of either our manufacturing plant or third party manufacturers with whom we contract for clinical and commercial supplies; or
- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or other regulatory authorities may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program altogether. Even if we do obtain regulatory approval, our product candidates may be approved for fewer or more limited indications than we request, approval may be contingent on the performance of costly post-marketing clinical trials, or approval may require labeling that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS or other regulatory authorities may require the establishment of a similar strategy, that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we believe our current or planned clinical trials are successful, regulatory authorities may not agree that our completed clinical trials provide adequate data on safety or efficacy. Approval by one regulatory authority does not ensure approval by any other regulatory authority. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for regulatory approvals and even if we file we may not receive the necessary approvals to commercialize our product candidates in any market.

If our product candidates obtain marketing approval, we will be subject to more extensive healthcare laws, regulation and enforcement and our failure to comply with those laws could have a material adverse effect on our results of operations and financial condition.

If we obtain approval in the U.S. for any of our product candidates, the regulatory requirements applicable to our operations, in particular our sales and marketing efforts, will increase significantly with respect to our operations and the potential for civil and criminal enforcement by the federal government and the states and foreign governments will increase with respect to the conduct of our business. The laws that may affect our operations in the U.S. include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving,
 offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service
 reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third party payors that are false or fraudulent;
- the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that prohibit
 executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes
 certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Patient Protection and Affordable Care Act ("PPACA"), which requires
 manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare and Medicaid Services
 ("CMS"), information related to payments and other transfers of value to physicians, other healthcare providers, and teaching
 hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family
 members;

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- foreign and state law equivalents of each of the above federal laws, such as the U.S. Foreign Corrupt Practices Act ("FCPA"), anti-kickback and false claims laws that may apply to items or services reimbursed by any third party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and
- the Trade Agreements Act ("TAA"), which requires that drugs sold to the U.S. Government must be manufactured in the U.S. or in TAA approved and designated countries. Drugs manufactured in countries not approved under the TAA, may not be sold to the U.S. without specific regulatory approval. We have little experience with this regulation and there is a risk that drugs made from Chinesemade API may not be sold to an entity of the U.S. such as the Veterans Health Administration ("VA") due to our inability to obtain regulatory approval. While there have been recent VA policy changes that appear to allow for sale of drugs from non-TAA approved countries, this policy may change or there may be additional policies or legislation that affect our ability to sell drug to the U.S. Government.

The scope of these laws and our lack of experience in establishing the compliance programs necessary to comply with this complex and evolving regulatory environment increases the risks that we may unknowingly violate the applicable laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results.

The impact of recent U.S. healthcare reform, its potential partial or full repeal, and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.

The commercial potential for our approved products could be affected by changes in healthcare spending and policy in the U.S. and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") altered Medicare coverage and payments for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. The MMA also provided authority for limiting the number of drugs that will be covered in any therapeutic class and as a result, we expect that there will be additional pressure to reduce costs. For example, the CMS in implementing the MMA has enacted regulations that reduced capitated payments to dialysis providers. These cost reduction initiatives and other provisions of the MMA could decrease the scope of coverage and the price that may be received for any approved dialysis products and could seriously harm our business and financial condition. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies have been enacted in many international markets which could similarly impact the commercial potential for our products.

Under the Medicare Improvements for Patients and Providers Act ("MIPPA"), a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by the CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage. It is unknown whether roxadustat, if approved in the U.S., will be included in the payment bundle. Under MIPPA, agents that have no IV equivalent in the bundle are currently expected to be excluded from the bundle until 2025. If roxadustat were included in the bundle, it may reduce the price that could be charged for roxadustat, and therefore potentially limit our profitability. Based on roxadustat's differentiated mechanism of action and therapeutic effects, and discussions with our collaboration partner, we currently believe that roxadustat might not be included in the bundle. If roxadustat is reimbursed outside of the bundle, it may potentially limit or delay market penetration of roxadustat.

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More recently, the PPACA was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The PPACA, among other things, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. In addition, other legislative changes have been proposed and adopted in the U.S. since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013.

It is likely that federal and state legislatures within the U.S. and foreign governments will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any products that may be approved for sale;
- the price and profitability of our products;
- pricing, coverage and reimbursement applicable to our products;
- the ability to successfully position and market any approved product; and
- the taxes applicable to our pharmaceutical product revenues.

Some of the provisions of the PPACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the PPACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. Given these possibilities and others we may not anticipate, the full extent to which our business, results of operations and financial condition could be adversely affected by the recent proposed legislation and the Executive Order is uncertain. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

Furthermore, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent regulatory approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We may not be able to conduct, or contract others to conduct, animal testing in the future, which could harm our research and development activities.

Certain laws and regulations relating to drug development require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted or delayed.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could result in significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failure to:

- comply with FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or comparable foreign regulatory authorities;
- · comply with manufacturing standards we have established;
- comply with privacy laws protecting personal information;
- comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities;
- comply with the FCPA and other anti-bribery laws;
- report financial information or data accurately;
- or disclose unauthorized activities to us.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, delays in clinical trials, or serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could harm our business, results of operations, financial condition and cash flows, including through the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations applicable to our operations in the U.S. and foreign countries. These current or future laws and regulations may impair our research, development or manufacturing efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our International Operations

We are establishing international operations and seeking approval to commercialize our product candidates outside of the U.S., in particular in China, and a number of risks associated with international operations could materially and adversely affect our business.

We expect to be subject to a number of risks related with our international operations, many of which may be beyond our control. These risks include:

- different regulatory requirements for drug approvals in foreign countries;
- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain countries;

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- · changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems and different competitive drugs indicated to treat the indications for which our product candidates are being developed;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- · compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- compliance with the FCPA, and other anti-corruption and anti-bribery laws;
- U.S. and foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- a reliance on CROs, clinical trial sites, principal investigators and other third parties that may be less experienced with clinical trials or have different methods of performing such clinical trials than we are used to in the U.S.;
- potential liability resulting from development work conducted by foreign distributors; and
- · business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. Refer to "Business - Government Regulation - Regulation in China" for a discussion of the regulatory requirements that are applicable to our current and planned business activities in China. In recent years, the regulatory framework in China regarding the pharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes. Any such changes or amendments may result in increased compliance costs on our business or cause delays in or prevent the successful development or commercialization of our product candidates in China. For example, the NMPA recently adopted the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use guidelines, and accordingly imposed regulatory oversight earlier in our production process for roxadustat manufactured and sold in China. The change in regulatory starting material triggered an extension of the inspection to our contract manufacturer STA, which was successfully completed in October 2018. In addition, Chinese authorities have become increasingly vigilant in enforcing laws in the pharmaceutical industry, in some cases launching industry-wide investigations, oftentimes appearing to focus on foreign companies. The costs and time necessary to respond to an investigation can be material. Any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China.

We plan to use our own manufacturing facilities in China to produce roxadustat API, roxadustat drug product, and FG-5200 corneal implants. As an organization, we have limited experience in the construction, licensure, and operation of a manufacturing plant, and accordingly we cannot assure you we will be able to meet regulatory requirements to operate our plant and to sell our products.

We have two manufacturing facilities in China, with one located in Beijing and the other in Cangzhou, Hebei. In December 2018, we received the Manufacturing License for Drug Substance and Drug Product for roxadustat and GMP certification for our Beijing facility that allows us to manufacture limited commercial quantities of roxadustat capsules. We are currently planning on manufacturing commercial-scale API at our Cangzhou facility, and expect to receive a license to produce roxadustat API at that site in the second half of 2019. However, as an organization, we have limited experience licensing and operating commercial manufacturing facilities.

We will be obligated to comply with continuing cGMP requirements and there can be no assurance that we will receive and maintain all of the appropriate licenses required to manufacture our product candidates for clinical and commercial use in China. In addition, we and our product suppliers must continually spend time, money and effort in production, record-keeping and quality assurance and appropriate controls in order to ensure that any products manufactured in our facilities meet applicable specifications and other requirements for product safety, efficacy and quality and there can be no assurance that our efforts will succeed for licensure or continue to be successful in meeting these requirements.

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We would require separate approval for the manufacture of FG-5200. In addition, we may convert the existing manufacturing process of FG-5200 to a semi-automated process, which may require us to show that implants from our new manufacturing process are comparable to the implants from our existing manufacturing process. There can be no assurance that we will successfully receive licensure and maintain approval for the manufacture of FG-5200, either of which would be expected to delay or preclude our ability to develop FG-5200 in China and may materially adversely affect our business and operations and prospects in China.

Manufacturing facilities in China are subject to periodic unannounced inspections by the NMPA and other regulatory authorities. We expect to depend on these facilities for our product candidates and business operations in China. Natural disasters or other unanticipated catastrophic events, including power interruptions, water shortages, storms, fires, earthquakes, terrorist attacks, government appropriation of our facilities, and wars, could significantly impair our ability to operate our manufacturing facilities. Certain equipment, records and other materials located in these facilities would be difficult to replace or would require substantial replacement lead time that would impact our ability to successfully commercialize our product candidates in China. The occurrence of any such event could materially and adversely affect our business, financial condition, results of operations, cash flows and prospects.

In addition to manufacturing, we are responsible for pharmacovigilance, medical affairs, and management of the third party distribution logistics for roxadustat in China. We have no experience in these areas as a company, and accordingly we cannot assure you we will be able to meet regulatory requirements or operate in these capacities successfully.

We are responsible for commercial manufacturing, pharmacovigilance, medical affairs, and management of the third party distribution logistics for roxadustat commercial activities in China. While we have been increasing our staffing in these areas, as a company, we have no experience managing or operating these functions for a commercial product and there can be no guarantee that we will do so efficiently or effectively. Mistakes or delays in these areas could limit our ability to successfully commercialize roxadustat in China, could limit our eventual market penetration, sales and profitability, and could subject us to significant liability in China.

Our decision to launch roxadustat in China prior to approval in the U.S. or Europe is largely unprecedented and could be subject to significant risk, delay and expense.*

Even though our subsidiary FibroGen Beijing has received marketing authorization for roxadustat for anemia caused by CKD in dialysis patients, we have not yet received approval in non-dialysis patients, and are awaiting the results from the Chinese authorities' completed inspection of our Phase 3 non-dialysis clinical trial sites.

We are currently expecting non-dialysis patients to be added to our approved dialysis label for roxadustat in China in the third quarter of 2019, and are planning on launching in the third quarter of 2019, however, it is possible that unforeseen delays in the China regulatory process could have a material adverse effect on our development and commercialization of roxadustat in China.

In addition we are required to conduct a 2,000 subject post-approval safety study to demonstrate the long-term safety of roxadustat and conduct intensive drug monitoring in an additional 1,000 patients, as well as provide period reporting to the authorities on GMP and quality compliance at our manufacturing facilities. If safety issues arise in this study, or generally after commercialization, our commercialization plans and profitability in China could be negatively impacted.

We and our collaboration partner in China, AstraZeneca, may experience difficulties in successfully generating sales of roxadustat in China.*

We and AstraZeneca have a profit sharing arrangement with respect to roxadustat in China and any difficulties we may experience in generating sales will affect our bottom line. Difficulties may be related to our ability to obtain reasonable pricing, reimbursement, hospital listing, and tendering, or other difficulties related to distribution, marketing, and sales efforts in China. Sales of roxadustat in China may be limited due to the complex nature of the healthcare system, low average personal income, pricing controls, still developing infrastructure and potentially rapid competition from other products. The government has committed to updating the National Reimbursement Drug List ("NRDL") in 2019. Previous updates to the NRDL occurred in 2017 and 2009. In addition, there were also NRDL price negotiations in 2018 for oncology drugs. Admission to the NRDL depends on a number of factors, including on-market experience, scale of patient adoption, physician endorsement, cost effectiveness and budget impact. Given that roxadustat was approved at the end of 2018, we may or may not qualify for the NRDL update in 2019. In particular, if we are unable to obtain reimbursement for roxadustat through the 2019 update to the NRDL, we may have to wait a substantial period of time before the reimbursement drug list is updated again. Without government reimbursement, many patients will not be able to afford roxadustat, since private commercial health insurance is rare, and our business and operations could be adversely affected. Therefore reimbursement and obtaining hospital listing is critical to roxadustat's near-term commercial success in China.

The market for treatment of anemia in CKD in China is highly competitive.

Although we have now received approval for roxadustat for the treatment of anemia caused by CKD in dialysis patients in China, and even if roxadustat receives approval for anemia caused by CKD in non-dialysis patients, it faces intense competition in the market for treatment of anemia in CKD. Roxadustat would compete with ESAs, which are offered by established multinational pharmaceutical companies such as Kyowa Hakko Kirin China Pharmaceutical Co., Ltd., Roche and Chinese pharmaceutical companies such as 3SBio Inc. and Di'ao Group Chengdu Diao Jiuhong Pharmaceutical Factory. Many of these competitors have substantially greater name recognition, scientific, financial, and marketing resources, as well as established distribution capabilities. Many of our competitors have more resources to develop or acquire, and more experience in developing or acquiring, new products and in creating market awareness for those products. Many of these competitors have significantly more experience than we have in navigating the Chinese regulatory framework regarding the development, manufacturing and marketing of drugs in China, as well as in marketing and selling anemia products in China. Additionally, we believe that most patients with anemia in CKD in China are currently being treated with traditional Chinese medicine, which is widely accepted and highly prevalent in China. Traditional Chinese medicine treatments are often oral and thus convenient and low-cost, and practitioners of traditional Chinese medicine are numerous and accessible in China. As a result, it may be difficult to persuade patients with anemia in CKD to switch from traditional Chinese medicine to roxadustat.

The Chinese government is implementing a new "Two Invoices" regulation which could affect the way we structure our distributorship relationships in China for roxadustat.

The Chinese government is implementing new regulations that impact distribution of pharmaceutical products in China. These regulations generally require that at most two invoices may be issued throughout the distribution chain. Failure to comply with the "Two-Invoices" regulations would prevent us from accessing the market in China. We are planning on modifying the distribution responsibilities under the China Agreement between AstraZeneca and FibroGen such that FibroGen would engage distributors and a third party logistics provider, and both companies will work together to manage the distribution network. FibroGen China Anemia Holdings, Ltd ("FibroGen China") has never managed distribution of pharmaceutical products, and this new distribution structure may impose higher costs or limit or delay our ability to sell products to our principal customers, and may limit the near term sales of our products.

There is no assurance that roxadustat will be included in the Medical Insurance Catalogs.

Eligible participants in the national basic medical insurance program in China, which consists of mostly urban residents, are entitled to reimbursement from the social medical insurance fund for up to the entire cost of medicines that are included in the Medical Insurance Catalogs. Refer to "Business - Government Regulation - Regulation in China." We believe that the inclusion of a drug in the Medical Insurance Catalogs can substantially improve the sales of a drug in China. The Ministry of Labor and Social Security in China ("MLSS") together with other government authorities, select medicines to be included in the Medical Insurance Catalogs based on a variety of factors, including treatment requirements, frequency of use, effectiveness and price. The MLSS also occasionally removes medicines from such catalogs. There can be no assurance that roxadustat will be included, and once included, remain in the Medical Insurance Catalogs. The exclusion or removal of roxadustat from the Medical Insurance Catalogs may materially and adversely affect sales of roxadustat.

Even if FG-5200 can be manufactured successfully and achieve regulatory approval, we may not achieve commercial success.

We have not yet received a license to manufacture FG-5200 in our Beijing manufacturing facility or at scale, and we will have to show that FG-5200 produced in our China manufacturing facility meets the applicable regulatory requirements. There can be no assurance that we can meet these requirements or that FG-5200 can be approved for development, manufacture and sale in China.

Even if we are able to manufacture and develop FG-5200 as a medical device in China, the size and length of any potential clinical trials required for approval are uncertain and we are unable to predict the time and investment required to obtain regulatory approval. Moreover, even if FG-5200 can be successfully developed for approval in China, our product candidate would require extensive training and investment in assisting physicians in the use of FG-5200.

The retail prices of any product candidates that we develop may be subject to control, including periodic downward adjustment, by Chinese government authorities.

The price for pharmaceutical products is highly regulated in China, both at the national and provincial level. Price controls may reduce prices to levels significantly below those that would prevail in less regulated markets, or limit the volume of products that may be sold, either of which may have a material and adverse effect on potential revenues from sales of roxadustat in China. Moreover, the process and timing for the implementation of price restrictions is unpredictable, which may cause potential revenues from the sales of roxadustat to fluctuate from period to period.

If our planned business activities in China fall within a restricted category under the China Catalog for Guidance for Foreign Investment, we will need to operate in China through a variable interest entity ("VIE") structure.

The China Catalog for Guidance for Foreign Investment sets forth the industries and sectors that the Chinese government encourages and restricts with respect to foreign investment and participation. The Catalog for Guidance for Foreign Investment is subject to revision from time to time by the China Ministry of Commerce. While we currently do not believe the development and marketing of roxadustat falls within a restricted category under the Catalog for Guidance for Foreign Investment, if roxadustat does fall under such a restricted category, we will need to operate in China through a VIE structure. A VIE structure involves a wholly foreign-owned enterprise that would control and receive the economic benefits of a domestic Chinese company through various contractual relationships. Such a structure would subject us to a number of risks that may have an adverse effect on our business, including that the Chinese government may determine that such contractual arrangements do not comply with applicable regulations, Chinese tax authorities may require us to pay additional taxes, shareholders of our VIEs may have potential conflicts of interest with us, and we may lose the ability to use and enjoy assets held by our VIEs that are important to the operations of our business if such entities go bankrupt or become subject to dissolution or liquidation proceedings. VIE structures in China have come under increasing scrutiny from accounting firms and the Securities and Exchange Commission ("SEC") staff. If we do attempt to use a VIE structure and are unsuccessful in structuring it so as to qualify as a VIE, we would not be able to consolidate the financial statements of the VIE with our financial statements, which could have a material adverse effect on our operating results and financial condition.

FibroGen Beijing would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.

We plan to conduct all of our business in China through FibroGen China and FibroGen Beijing. We may rely on dividends and royalties paid by FibroGen Beijing for a portion of our cash needs, including the funds necessary to service any debt we may incur and to pay our operating expenses. The payment of dividends by FibroGen Beijing is subject to limitations. Regulations in China currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in China. FibroGen Beijing is not permitted to distribute any profits until losses from prior fiscal years have been recouped and in any event must maintain certain minimum capital requirements. FibroGen Beijing is also required to set aside at least 10.0% of its after-tax profit based on Chinese accounting standards each year to its statutory reserve fund until the cumulative amount of such reserves reaches 50.0% of its registered capital. Statutory reserves are not distributable as cash dividends. In addition, if FibroGen Beijing incurs debt on its own behalf in the future, the agreements governing such debt may restrict its ability to pay dividends or make other distributions to us. As of June 30, 2019, approximately \$5.1 million of our cash and cash equivalents is held in China.

Any capital contributions from us to FibroGen Beijing must be approved by the Ministry of Commerce in China, and failure to obtain such approval may materially and adversely affect the liquidity position of FibroGen Beijing.

The Ministry of Commerce in China or its local counterpart must approve the amount and use of any capital contributions from us to FibroGen Beijing, and there can be no assurance that we will be able to complete the necessary government registrations and obtain the necessary government approvals on a timely basis, or at all. If we fail to do so, we may not be able to contribute additional capital to fund our Chinese operations, and the liquidity and financial position of FibroGen Beijing may be materially and adversely affected.

We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.

If roxadustat is approved for sale in China, most of our product sales will occur in local Chinese currency and our operating results will be subject to volatility from currency exchange rate fluctuations. To date, we have not hedged against the risks associated with fluctuations in exchange rates and, therefore, exchange rate fluctuations could have an adverse impact on our future operating results. Changes in value of the Renminbi against the U.S. dollar, Euro and other currencies is affected by, among other things, changes in China's political and economic conditions. Currently, the Renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. Any significant currency exchange rate fluctuations may have a material adverse effect on our business and financial condition.

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In addition, the Chinese government imposes controls on the convertibility of the Renminbi into foreign currencies and the remittance of foreign currency out of China for certain transactions. Shortages in the availability of foreign currency may restrict the ability of FibroGen Beijing to remit sufficient foreign currency to pay dividends or other payments to us, or otherwise satisfy their foreign currency-denominated obligations. Under existing Chinese foreign exchange regulations, payments of current account items, including profit distributions, interest payments and balance of trade, can be made in foreign currencies without prior approval from the State Administration of Foreign Exchange ("SAFE") by complying with certain procedural requirements. However, approval from SAFE or its local branch is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The Chinese government may also at its discretion restrict access in the future to foreign currencies for current account transactions. If the foreign exchange control system prevents us from obtaining sufficient foreign currency to satisfy our operational requirements, our liquidity and financial position may be materially and adversely affected.

Because FibroGen Beijing's funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen Beijing deposits its funds could adversely affect our business.

Banks and other financial institutions in China do not provide insurance for funds held on deposit. As a result, in the event of a bank failure, FibroGen Beijing may not have access to funds on deposit. Depending upon the amount of money FibroGen Beijing maintains in a bank that fails, its inability to have access to cash could materially impair its operations.

We may be subject to tax inefficiencies associated with our offshore corporate structure.

The tax regulations of the U.S. and other jurisdictions in which we operate are extremely complex and subject to change. New laws, new interpretations of existing laws, such as the Base Erosion Profit Shifting project initiated by the Organization for Economic Co-operation and Development, and any legislation proposed by the relevant taxing authorities, or limitations on our ability to structure our operations and intercompany transactions may lead to inefficient tax treatment of our revenue, profits, royalties, and distributions, if any are achieved.

In addition, we and our foreign subsidiaries have various intercompany transactions. We may not be able to obtain certain benefits under relevant tax treaties to avoid double taxation on certain transactions among our subsidiaries. If we are not able to avail ourselves to the tax treaties, we could be subject to additional taxes, which could adversely affect our financial condition and results of operations.

On December 22, 2017, the U.S. enacted the Tax Cuts and Jobs Act ("Tax Act") that instituted fundamental changes to the taxation of multinational corporations. The Tax Act includes changes to the taxation of foreign earnings by implementing a dividend exemption system, expansion of the current anti-deferral rules, a minimum tax on low-taxed foreign earnings and new measures to deter base erosion. The Tax Act also includes a permanent reduction in the corporate tax rate to 21%, repeal of the corporate alternative minimum tax, expensing of capital investment, and limitation of the deduction for interest expense. Furthermore, as part of the transition to the new tax system, a one-time transition tax is imposed on a U.S. shareholder's historical undistributed earnings of foreign affiliates. Although the Tax Act is generally effective January 1, 2018, GAAP requires recognition of the tax effects of new legislation during the reporting period that includes the enactment date, which was December 22, 2017.

As a result of the impacts of the Tax Act, the SEC provided guidance that allows us to record provisional amounts for those impacts, with the requirement that the accounting be completed in a period not to exceed one year from the date of enactment. As of December 31, 2018, we completed our analysis of the accounting for the tax effects of the Tax Act and no material adjustments were recognized as of December 31, 2018. The primary impact of the Tax Act relates to the re-measurement of deferred tax assets and liabilities resulting from the change in the corporate tax rate ("Corporate Tax Rate Change"), which was recorded as of December 2017. Developing interpretations of the provisions of the Tax Act, changes to U.S. Treasury regulations, administrative interpretations, or court decisions interpreting the Tax Act in the future periods may require further adjustments to our analysis.

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Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.

We seek to protect the products and technology that we consider important to our business by pursuing patent applications in China and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. We note that the filing of a patent application does not mean that we will be granted a patent, or that any patent eventually granted will be as broad as requested in the patent application or will be sufficient to protect our technology. There are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications not to be granted, including known or unknown prior art, deficiencies in the patent application, or lack of originality of the technology. Furthermore, the terms of our patents are limited. The patents we hold and the patents that may be granted from our currently pending patent applications have, absent any patent term adjustment or extension, a twenty-year protection period starting from the date of application.

Intellectual property rights and confidentiality protections in China may not be as effective as those in the U.S. or other countries for many reasons, including lack of procedural rules for discovery and evidence, low damage awards, and lack of judicial independence. Implementation and enforcement of China intellectual property laws have historically been deficient and ineffective and may be hampered by corruption and local protectionism. Policing unauthorized use of proprietary technology is difficult and expensive, and we may need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability and validity of our proprietary rights or those of others. The experience and capabilities of China courts in handling intellectual property litigation varies and outcomes are unpredictable. An adverse determination in any such litigation could materially impair our intellectual property rights and may harm our business.

We are subject to laws and regulations governing corruption, which will require us to develop, maintain, and implement costly compliance programs.

We must comply with a wide range of laws and regulations to prevent corruption, bribery, and other unethical business practices, including the FCPA, anti-bribery and anti-corruption laws in other countries, particularly China. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

Anti-bribery laws prohibit us, our employees, and some of our agents or representatives from offering or providing any personal benefit to covered government officials to influence their performance of their duties or induce them to serve interests other than the missions of the public organizations in which they serve. Certain commercial bribery rules also prohibit offering or providing any personal benefit to employees and representatives of commercial companies to influence their performance of their duties or induce them to serve interests other than their employers. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with these anti-bribery laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the anti-bribery laws present particular challenges in the pharmaceutical industry because in many countries including China, hospitals are state-owned or operated by the government, and doctors and other hospital employees are considered foreign government officials. Furthermore, in certain countries (China in particular), hospitals and clinics are permitted to sell pharmaceuticals to their patients and are primary or significant distributors of pharmaceuticals. Certain payments to hospitals in connection with clinical studies, procurement of pharmaceuticals and other work have been deemed to be improper payments to government officials that have led to vigorous anti-bribery law enforcement actions and heavy fines in multiple jurisdictions, particularly in the U.S. and China.

It is not always possible to identify and deter violations, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

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In the pharmaceutical industry, corrupt practices include, among others, acceptance of kickbacks, bribes or other illegal gains or benefits by the hospitals and medical practitioners from pharmaceutical manufacturers, distributors or their third party agents in connection with the prescription of certain pharmaceuticals. If our employees, affiliates, distributors or third party marketing firms violate these laws or otherwise engage in illegal practices with respect to their sales or marketing of our products or other activities involving our products, we could be required to pay damages or heavy fines by multiple jurisdictions where we operate, which could materially and adversely affect our financial condition and results of operations. The Chinese government has also sponsored anti-corruption campaigns from time to time, which could have a chilling effect on any future marketing efforts by us to new hospital customers. There have been recent occurrences in which certain hospitals have denied access to sales representatives from pharmaceutical companies because the hospitals wanted to avoid the perception of corruption. If this attitude becomes widespread among our potential customers, our ability to promote our products to hospitals may be adversely affected.

As we expand our operations in China and other jurisdictions internationally, we will need to increase the scope of our compliance programs to address the risks relating to the potential for violations of the FCPA and other anti-bribery and anti-corruption laws. Our compliance programs will need to include policies addressing not only the FCPA, but also the provisions of a variety of anti-bribery and anti-corruption laws in multiple foreign jurisdictions, including China, provisions relating to books and records that apply to us as a public company, and include effective training for our personnel throughout our organization. The creation and implementation of anti-corruption compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. Violation of the FCPA and other anti-corruption laws can result in significant administrative and criminal penalties for us and our employees, including substantial fines, suspension or debarment from government contracting, prison sentences, or even the death penalty in extremely serious cases in certain countries. The SEC also may suspend or bar us from trading securities on U.S. exchanges for violation of the FCPA's accounting provisions. Even if we are not ultimately punished by government authorities, the costs of investigation and review, distraction of our personnel, legal defense costs, and harm to our reputation could be substantial and could limit our profitability or our ability to develop or commercialize our product candidates. In addition, if any of our competitors are not subject to the FCPA, they may engage in practices that will lead to their receipt of preferential treatment from foreign hospitals and enable them to secure business from foreign hospitals in ways that are unavailable to us.

Uncertainties with respect to the China legal system could have a material adverse effect on us.

The legal system of China is a civil law system primarily based on written statutes. Unlike in a common law system, prior court decisions may be cited for reference but are not binding. Because the China legal system continues to rapidly evolve, the interpretations of many laws, regulations and rules are not always uniform and enforcement of these laws, regulations and rules involve uncertainties, which may limit legal protections available to us. Moreover, decision makers in the China judicial system have significant discretion in interpreting and implementing statutory and contractual terms, which may render it difficult for FibroGen Beijing to enforce the contracts it has entered into with our business partners, customers and suppliers. Different government departments may have different interpretations of certain laws and regulations, and licenses and permits issued or granted by one government authority may be revoked by a higher government authority at a later time. Navigating the uncertainty and change in the China legal system will require the devotion of significant resources and time, and there can be no assurance that our contractual and other rights will ultimately be enforced.

Changes in China's economic, political or social conditions or government policies could have a material adverse effect on our business and operations.*

Chinese society and the Chinese economy continue to undergo significant change. Changes in the regulatory structure, regulations, and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy, but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the regulatory structure and structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes and structural changes, any of which could materially and adversely affect FibroGen Beijing's development and commercialization timelines, liquidity, access to capital, and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China. In addition, the changing government regulations and policies could result in delays and cost increases to our development, manufacturing, approval, and commercialization timelines in China.

Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may materially and adversely affect our business, financial condition and results of operations.

We are subject to China Labor Contract Law, which provides strong protections for employees and imposes many obligations on employers. The Labor Contract Law places certain restrictions on the circumstances under which employers may terminate labor contracts and require economic compensation to employees upon termination of employment, among other things. In addition, companies operating in China are generally required to contribute to labor union funds and the mandatory social insurance and housing funds. Any failure by us to comply with Chinese labor and social insurance laws may subject us to late fees, fines and penalties, or cause the suspension or termination of our ability to conduct business in China, any of which could have a material and adverse effect on business, results of operations and prospects.

Recent developments relating to the United Kingdom's referendum vote in favor of leaving the EU could adversely affect us.

The United Kingdom held a referendum on June 23, 2016 in which a majority voted for the United Kingdom's withdrawal from the EU, commonly referred to as "Brexit". As a result of this vote, negotiations are expected to commence to determine the terms of the United Kingdom's withdrawal from the EU as well as its relationship with the EU going forward, including the terms of trade between the United Kingdom and the EU. The effects of the United Kingdom's withdrawal from the EU, and the perceptions as to its impact, are expected to be far-reaching and may adversely affect business activity and economic conditions in Europe and globally and could continue to contribute to instability in global financial markets, including foreign exchange markets. The United Kingdom's withdrawal from the EU could also have the effect of disrupting the free movement of goods, services and people between the United Kingdom and the EU and could also lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which EU laws to replace or replicate, including laws that could impact our ability, or our collaborator's ability in the case of roxadustat, to obtain approval of our products or sell our products in the United Kingdom. However, the full effects of such withdrawal are uncertain and will depend on any agreements the United Kingdom may make to retain access to EU markets. Lastly, as a result of the United Kingdom's withdrawal from the EU, other European countries may seek to conduct referenda with respect to their continuing membership with the EU. Given these possibilities and others we may not anticipate, as well as the lack of comparable precedent, the full extent to which our business, results of operations and financial condition could be adversely affected by the United Kingdom's withdrawal from the EU is uncertain

Risks Related to the Operation of Our Business

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, commercialization and administration capabilities or contract with third parties to provide these capabilities for us. As our operations expand and we continue to undertake the efforts and expense to operate as a public reporting company, we expect that we will need to increase the responsibilities on members of management in order to manage any future growth effectively. Our failure to accomplish any of these steps could prevent us from successfully implementing our strategy and maintaining the confidence of investors in our Company.

If we fail to attract and keep senior management and key personnel, in particular our chief executive officer, we may be unable to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

We are highly dependent on our chief executive officer, Thomas B. Neff, and other members of our senior management team. The loss of the services of Mr. Neff or any of these other individuals would be expected to significantly negatively impact the development and commercialization of our product candidates, our existing collaborative relationships and our ability to successfully implement our business strategy.

Recruiting and retaining qualified commercial, development, scientific, clinical, and manufacturing personnel are and will continue to be critical to our success, particularly as we expand our commercialization operations. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

There is also significant competition, in particular in the San Francisco Bay Area, for the hiring of experienced and qualified personnel, which increases the importance of retention of our existing personnel. If we are unable to continue to attract and retain personnel with the quality and experience applicable to our product candidates, our ability to pursue our strategy will be limited and our business and operations would be adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing, manufacturing and commercialization of our product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under state consumer protection acts. If we are unable to obtain insurance coverage at levels that are appropriate to maintain our business and operations, or if we are unable to successfully defend ourselves against product liability claims, we may incur substantial liabilities or otherwise cease operations. Product liability claims may result in:

- · termination of further development of unapproved product candidates or significantly reduced demand for any approved products;
- material costs and expenses to defend the related litigation;
- a diversion of time and resources across the entire organization, including our executive management;
- product recalls, withdrawals or labeling restrictions;
- · termination of our collaboration relationships or disputes with our collaboration partners; and
- reputational damage negatively impacting our other product candidates in development.

If we fail to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, we may not be able to continue to develop our product candidates. We maintain product liability insurance in a customary amount for the stage of development of our product candidates. Although we believe that we have sufficient coverage based on the advice of our third party advisors, there can be no assurance that such levels will be sufficient for our needs. Moreover, our insurance policies have various exclusions, and we may be in a dispute with our carrier as to the extent and nature of our coverage, including whether we are covered under the applicable product liability policy. If we are not able to ensure coverage or are required to pay substantial amounts to settle or otherwise contest the claims for product liability, our business and operations would be negatively affected.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, collaboration partners, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We upgraded our disaster and data recovery capabilities in June 2017, however, to the extent that any disruption or security breach, in particular with our partners' operations, results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and it could result in a material disruption and delay of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

We depend on sophisticated information technology systems to operate our business and a cyber-attack or other breach of these systems could have a material adverse effect on our business.

We rely on information technology systems to process, transmit and store electronic information in our day-to-day operations. The size and complexity of our information technology systems makes them vulnerable to a cyber-attack, malicious intrusion, breakdown, destruction, loss of data privacy or other significant disruption. While we have recently upgraded our disaster data recovery program, a successful attack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyber-attacks are becoming more sophisticated and frequent. We have invested in our systems and the protection and recoverability of our data to reduce the risk of an intrusion or interruption, and we monitor and test our systems on an ongoing basis for any current or potential threats. There can be no assurance that these measures and efforts will prevent future interruptions or breakdowns. If we fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to these systems, we could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows.

Our headquarters and data storage facilities are located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business, results of operations and financial condition.

We and some of the third party service providers on which we depend for various support functions, such as data storage, are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires.

We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, or otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place are unlikely to provide adequate protection in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above your purchase price.

In general, pharmaceutical, biotechnology and other life sciences company stocks have been highly volatile in the current market. The volatility of pharmaceutical, biotechnology and other life sciences company stocks is sometimes unrelated to the operating performance of particular companies and biotechnology and life science companies stocks often respond to trends and perceptions rather than financial performance. In particular, the market price of shares of our common stock could be subject to wide fluctuations in response to the following factors:

- results of clinical trials of our product candidates, including roxadustat and pamrevlumab;
- the timing of the release of results of and regulatory updates regarding our clinical trials;
- the level of expenses related to any of our product candidates or clinical development programs;
- results of clinical trials of our competitors' products;
- safety issues with respect to our product candidates or our competitors' products;
- regulatory actions with respect to our product candidates and any approved products or our competitors' products;
- fluctuations in our financial condition and operating results, which will be significantly affected by the manner in which we recognize revenue from the achievement of milestones under our collaboration agreements;
- adverse developments concerning our collaborations and our manufacturers;
- the termination of a collaboration or the inability to establish additional collaborations;
- the publication of research reports by securities analysts about us or our competitors or our industry or negative recommendations or withdrawal of research coverage by securities analysts;
- the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- the ineffectiveness of our internal controls;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;

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- additions and departures of key personnel;
- announced strategic decisions by us or our competitors;
- · changes in legislation or other regulatory developments affecting our product candidates or our industry;
- fluctuations in the valuation of the biotechnology industry and particular companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other stockholders;
- speculation in the press or investment community;
- announcement or expectation of additional financing efforts;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- changes in accounting principles;
- activities of the government of China, including those related to the pharmaceutical industry as well as industrial policy generally;
- performance of other U.S. publicly traded companies with significant operations in China;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters such as earthquakes and other calamities;
- changes in market conditions for biopharmaceutical stocks;
- changes in general market and economic conditions; and
- the other factors described in this "Risk Factors" section.

As a result of fluctuations caused by these and other factors, comparisons of our operating results across different periods may not be accurate indicators of our future performance. Any fluctuations that we report in the future may differ from the expectations of market analysts and investors, which could cause the price of our common stock to fluctuate significantly. Moreover, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources, and could also require us to make substantial payments to satisfy judgments or to settle litigation.

We have broad discretion in the use of the remaining net proceeds from our underwritten public offerings of common stock completed on April 11, 2017 (the "April 2017 Offering") and August 24, 2017 (the "August 2017 Offering") and may not use them effectively.

The net proceeds from the April 2017 Offering is intended to be used to fund the expansion of product development in China, including developing roxadustat in additional indications beyond CKD, manufacturing and commercialization activities, as well as for general corporate purposes. The net proceeds from the August 2017 Offering is intended to be used to fund the expansion of product development, including our development of pamrevlumab through Phase 3 trials, manufacturing and commercialization activities, as well as for general corporate purposes. These general corporate purposes, may include, among other things, funding research and development, clinical trials, vendor payables, potential regulatory submissions, hiring additional personnel and capital expenditures. However, we have no current commitments or obligations to use the net proceeds in the manner described above. Our management has broad discretion in the application of the remaining net proceeds from the April 2017 Offering and the August 2017 Offering, and could spend the remaining net proceeds in ways our stockholders may not agree with or that fails to improve our business or enhance the value of our common stock. The failure by our management to use these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates.

If securities or industry analysts do not continue to publish research or reports about our business, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock, our stock price would likely decline. If one or more of these analysts cease coverage of our Company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.*

As of July 31, 2019, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 39.03% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date and shares issuable upon settlement of restricted stock units that will vest within 60 days after such date. This percentage is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G, if any, filed with the SEC, which information may not be accurate as of April 30, 2019. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. The interests of this group may differ from those of other stockholders and they may vote their shares in a way that is contrary to the way other stockholders vote their shares. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

Additional remedial measures that may be imposed in the proceedings instituted by the SEC against five China based accounting firms, including the Chinese affiliate of our independent registered public accounting firm, could result in our consolidated financial statements being determined to not be in compliance with the requirements of the Exchange Act.

In late 2012, the SEC commenced administrative proceedings under Rule 102(e) of its Rules of Practice and also under the Sarbanes-Oxley Act of 2002 against the Chinese affiliates of the "big four" accounting firms, including PricewaterhouseCoopers Zhong Tian CPAs Limited, the Chinese affiliate of our independent registered public accounting firm. The Rule 102(e) proceedings initiated by the SEC relate to these firms' failure to produce documents, including audit work papers, in response to the request of the SEC pursuant to Section 106 of the Sarbanes-Oxley Act of 2002, as the auditors located in China are not in a position lawfully to produce documents directly to the SEC because of restrictions under Chinese law and specific directives issued by the China Securities Regulatory Commission ("CSRC"). The issues raised by the proceedings are not specific to our auditors or to us.

In January 2014, an administrative law judge reached an initial decision that the Chinese affiliates of the "big four" accounting firms should be barred from practicing before the SEC for a period of six months. In February 2015, the Chinese affiliates of the "big four" accounting firms each agreed to a censure and to pay a fine to the SEC to settle the dispute and avoid suspension of their ability to practice before the SEC and audit U.S.-listed companies. The settlement required the firms to follow detailed procedures and to seek to provide the SEC with access to Chinese firms' audit documents via the CSRC. If future document productions fail to meet specified criteria, the SEC retains authority to impose a variety of additional remedial measures on the firms depending on the nature of the failure.

We cannot predict if the SEC will further review the four firms' compliance with specified criteria or if such further review would result in the SEC imposing additional penalties such as suspensions or commencing any further administrative proceedings. Although it does not play a substantial role (as defined under PCAOB standards) in the audit of our consolidated financial statements, if PricewaterhouseCoopers Zhong Tian CPAs Limited were denied, temporarily, the ability to practice before the SEC, our ability to produce audited consolidated financial statements for our Company could be affected and we could be determined not to be in compliance with the requirements of the Exchange Act. Such a determination could ultimately lead to the delisting of our shares from the Nasdaq Global Select Market or deregistration from the SEC, or both, which would substantially reduce or effectively terminate the trading of our stock.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our business, results of operations, financial condition and cash flows and future prospects.

While we currently have no specific plans to acquire any other businesses, we may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our present or future product candidates and business or otherwise offer opportunities for our Company. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our existing stockholders' percentage of ownership;
- incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

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We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- · problems integrating the purchased business, products or technologies, or employees or other assets of the acquisition target;
- · increases to our expenses;
- disclosed or undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- reprioritization of our development programs and even cessation of development and commercialization of our current product candidates;
- · harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current directors or management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- · create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a
 majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed prior to the end of their term only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum:
- require a supermajority vote of the holders of our common stock or the majority vote of our board of directors to amend our bylaws;
 and
- require a supermajority vote of the holders of our common stock to amend the classification of our board of directors into three classes and to amend certain other provisions of our certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

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Moreover, because we are incorporated in Delaware, we are governed by certain anti-takeover provisions under Delaware law which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. We are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Changes in our tax provision or exposure to additional tax liabilities could adversely affect our earnings and financial condition.

As a multinational corporation, we are subject to income taxes in the U.S. and various foreign jurisdictions. Significant judgment is required in determining our global provision for income taxes and other tax liabilities. In the ordinary course of a global business, there are intercompany transactions and calculations where the ultimate tax determination is uncertain. Our income tax returns are subject to audits by tax authorities. Although we regularly assess the likelihood of adverse outcomes resulting from these examinations to determine our tax estimates, a final determination of tax audits or tax disputes could have an adverse effect on our results of operations and financial condition.

We are also subject to non-income taxes, such as payroll, sales, use, value-added, net worth, property, gross receipts, and goods and services taxes in the U.S., state and local, and various foreign jurisdictions. We are subject to audit and assessments by tax authorities with respect to these non-income taxes and may have exposure to additional non-income tax liabilities, which could have an adverse effect on our results of operations and financial condition.

On December 22, 2017, the U.S. enacted the Tax Act that instituted fundamental changes to the taxation of multinational corporations. The Tax Act includes changes to the taxation of foreign earnings by implementing a dividend exemption system, expansion of the current anti-deferral rules, a minimum tax on low-taxed foreign earnings and new measures to deter base erosion. The Tax Act also includes a permanent reduction in the corporate tax rate to 21%, repeal of the corporate alternative minimum tax, expensing of capital investment, and limitation of the deduction for interest expense. Furthermore, as part of the transition to the new tax system, a one-time transition tax is imposed on a U.S. shareholder's historical undistributed earnings of foreign affiliates. Although the Tax Act is generally effective January 1, 2018, GAAP requires recognition of the tax effects of new legislation during the reporting period that includes the enactment date, which was December 22, 2017.

As a result of the impact of the Tax Act, the SEC provided guidance that allows us to record provisional amounts for those affected items, with the requirement that the accounting be completed in a period not to exceed one year from the date of enactment. As of December 31, 2018, we completed our analysis of the accounting for the tax effects of the Tax Act and no material adjustments were recognized at year end. The primary impact of the Tax Act relates to the re-measurement of deferred tax assets and liabilities resulting from the Corporate Tax Rate Change, which was recorded as of December 31, 2017. Developing interpretations of the provisions of the Tax Act, changes to U.S. Treasury regulations, administrative interpretations or court decisions interpreting the Tax Act in the future periods may require further adjustments to our analysis.

Our amended and restated certificate of incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

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Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in our product candidates and maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS.

Use of Proceeds from Initial Public Offering of Common Stock

On November 13, 2014, our Registration Statement on Form S-1, as amended (Reg. Nos. 333-199069 and 333-200189) was declared effective in connection with the initial public offering of our common stock. There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on November 14, 2014.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES.

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

ITEM 5. OTHER INFORMATION.

None.

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ITEM 6. EXHIBITS

Exhibit		Incorporation By Reference			
Number	Exhibit Description	Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of FibroGen, Inc.	8-K	001-36740	3.1	11/21/2014
3.2	Amended and Restated Bylaws of FibroGen, Inc.	S-1/A	333-199069	3.4	10/23/2014
4.1	Form of Common Stock Certificate.	8-K	001-36740	4.1	11/21/2014
4.2	Investor Rights Agreement by and among FibroGen, Inc. and certain	S-1	333-199069	4.2	10/01/2014
	of its stockholders, dated as of December 1995.				
4.3	Investor Rights Agreement by and among FibroGen, Inc. and certain	S-1	333-199069	4.7	10/01/2014
	of its warrant holders, dated as of February 8, 2000.				
4.4	Warrant to Purchase 11,076 Shares of Common Stock issued to	S-1	333-199069	4.12	10/01/2014
	Bristow Investments, L.P, dated as of February 8, 2000.				
4.5	Common Stock Purchase Agreement by and between FibroGen, Inc.	S-1/A	333-199069	4.17	10/24/2014
	and AstraZeneca AB, dated as of October 20, 2014.				
4.6	Shareholders' Agreement by and among FibroGen International	10-Q	001-36740	4.6	11/8/2017
	(Cayman) Limited and certain of its shareholders, dated as of				
10.6%	September 8, 2017.				
10.6*+	FibroGen, Inc. Non-Employee Director Compensation Policy, as amended.	-	-	-	-
31.1*	Certification of Chief Executive Officer, as required by Rule 13a-14(a)				
31.1	or Rule 15d-14(a).	-	-	-	-
31.2*	Certification of Chief Financial Officer, as required by Rule 13a-14(a)	_	_	_	_
31.2	or Rule 15d-14(a).				
32.1*	Certification of Principal Executive Officer and Principal Financial	_	_	_	_
52.1	Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section				
	1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C.				
	<u>§1350)(1)).</u>				
101.INS	Inline XBRL Instance Document	-	-	-	-
101.SCH	Inline XBRL Taxonomy Extension Schema Document	-	-	-	-
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	-	-	-	-
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	-	-	-	-
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	-	-	-	-
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	-	-	-	-
104	Cover Page Interactive Data File (formatted as inline XBRL with	-	-	-	-
	applicable taxonomy extension information contained in Exhibits				
	101.*)				
* E:1 11					

^{*} Filed herewith

⁺ Indicates a management contract or compensatory plan

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Dated: August 8, 2019

Dated: August 8, 2019

FibroGen, Inc.

By: /s/ Thomas B. Neff

Thomas B. Neff
Chairman of the Board and Chief Executive Officer

(Principal Executive Officer)

By: /s/ Pat Cotroneo

Pat Cotroneo

Senior Vice President, Finance and Chief Financial Officer (Principal Financial and Accounting Officer)

Exhibit 31.1

CERTIFICATION

- I, Thomas B. Neff, certify that;
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 8, 2019

/s/ Thomas B. Neff

Thomas B. Neff Chairman of the Board and Chief Executive Officer (Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

- I, Pat Cotroneo, certify that;
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 8, 2019

/s/ Pat Cotroneo
Pat Cotroneo

Senior Vice President, Finance and Chief Financial Officer (Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended ("Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Thomas B. Neff, Chief Executive Officer of FibroGen, Inc. ("the Company"), and Pat Cotroneo, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

- 1. The Company's Quarterly Report on Form 10-Q for the period ended June 30, 2019, to which this Certification is attached as Exhibit 32.1 ("Periodic Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and
- 2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: August 8, 2019

IN WITNESS WHEREOF, the undersigned have set their hands hereto as of the 8th day of August, 2019.

 /s/ Thomas B. Neff
 /s/ Pat Cotroneo

 Thomas B. Neff
 Pat Cotroneo

 Chairman of the Board and Chief Executive Officer
 Senior Vice President, Finance and Chief Financial Officer

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of FibroGen, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

EXHIBIT P



Investors and Media

Press Release



Tiew printer-friendly version

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FibroGen Announces Positive Phase 3 Pooled Roxadustat Safety and Efficacy Results for Treatment of Anemia in Chronic Kidney Disease

Roxadustat cardiovascular safety comparable to placebo in non-dialysis dependent (NDD) patients, as assessed by Major Adverse Cardiovascular Events (MACE) and MACE+

Roxadustat did not increase risk of MACE and reduced risk of MACE+ compared to epoetin alfa in dialysis-dependent (DD) patients;

Roxadustat reduced risk of MACE by 30% and MACE+ by 34% compared to epoetin alfa in the incident dialysis (ID) patient subgroup of the DD population

Roxadustat achieved primary efficacy endpoints in NDD and DD patients

WASHINGTON, Nov. 08, 2019 (GLOBE NEWSWIRE) -- FibroGen, Inc. (NASDAQ:FGEN), today announced results from the pooled analyses of data from six global pivotal Phase 3 trials investigating roxadustat, a first-in-class, orally-administered inhibitor of hypoxia-inducible-factor (HIF) prolyl hydroxylase activity. The pooled analyses assessed the safety and efficacy of roxadustat as a treatment for anemia in chronic kidney disease (CKD) compared to placebo in Non-Dialysis-Dependent (NDD) patients and to standard of care epoetin alfa in Dialysis-Dependent (DD) patients, including the clinically important Incident Dialysis (ID) patient subgroup. These Phase 3 trials conducted by FibroGen and collaboration partners AstraZeneca and Astellas Pharma, Inc., enrolled over 8,000 CKD patients from more than 50 countries.

"The pooled safety analyses assessing roxadustat as a treatment for anemia in chronic kidney disease demonstrate a cardiovascular safety profile comparable with placebo in patients not on dialysis, and comparable or in some cases better than that of epoetin alfa in patients on dialysis," said Robert Provenzano, MD, Associate Professor of Medicine, Wayne State University, Detroit, Michigan, U.S. and a primary investigator on the global Phase 3 program. "It is exciting to see this application of the groundbreaking science on oxygen sensing and adaptation to hypoxia recently awarded the 2019 Nobel Prize in Physiology or Medicine, and championed by FibroGen's late founder and CEO, Tom Neff, who sadly passed away earlier this year. These positive safety results, coupled with roxadustat's well-defined efficacy in CKD patients, and its oral formulation, support the potential for roxadustat to become an important new treatment option for patients with anemia associated with CKD."

These late-breaking data were featured in the High-Impact Clinical Trials oral abstract session on Friday, November 8, at the American Society of Nephrology Kidney Week 2019 in Washington, D.C. (Presentation FR-OR131)

Pooled Efficacy Results

Individually, all six Phase 3 trials included in these pooled analyses (OLYMPUS, ANDES, ALPS, HIMALAYAS, SIERRAS, and ROCKIES) achieved the primary efficacy endpoint of mean hemoglobin (Hb) change from baseline compared to placebo in patients not on dialysis and to epoetin alfa in patients on dialysis.

In the pooled analysis of Non-Dialysis Dependent (NDD) patients (n=4277):

- Roxadustat was statistically superior to placebo, demonstrating an improvement of 1.85 g/dL in patients' Hb levels from baseline to the average over 28-52 weeks compared to 0.13 g/dL among patients in the placebo arm, for an overall treatment difference of 1.72 g/dL (p<0.001).
- The rate of rescue therapy required in the first year of treatment among patients treated with roxadustat (8.9%) was less than one third of the rate of the placebo arm (31.1%) p<0.0001; HR=0.19 (95% CI: 0.16, 0.23).
- The rate of red blood cell (RBC) transfusions required in the first year of treatment was also lower with roxadustat (5.2%) than placebo (15.4%) p<0.0001; HR=0.26 (95% CI: 0.21, 0.32).

- Roxadustat was statistically superior to epoetin alfa, demonstrating an improvement of 1.22 g/dL in patients' Hb levels from baseline to the average over 28-52 weeks compared to 0.99 g/dL, for an overall treatment difference of 0.23 g/dL (p<0.0001).
- Roxadustat was superior to epoetin alfa across patients regardless of inflammation status, categorized by the baseline CRP levels (CRP > 4.9 mg/L), demonstrating an improvement of 1.29 g/dL and 1.27 g/dL in Hb levels from baseline in patients with and without inflammation, respectively, compared to 0.96 g/dL and 1.05 g/dL with epoetin alfa.
- The rate of RBC transfusions required in the first year of treatment was also lower with roxadustat (9.5%) than with epoetin alfa (12.8%) in DD patients (p=0.046). HR=0.82 (95% CI: 0.679, 0.997).

Across the NDD and DD patient populations, roxadustat was effective in raising Hb levels regardless of whether patients were iron-replete (i.e., shown to have sufficient stores of iron in their body, TSAT% ≥20% and Ferritin ≥100 ng/mL) at baseline. NDD patients experienced a mean change of 1.94 g/dL from baseline with roxadustat in both iron-replete and non-replete subpopulations, compared to 0.13 g/dL in iron-replete and 0.33 g/dL in non-replete patients receiving placebo.

Pooled Safety Results

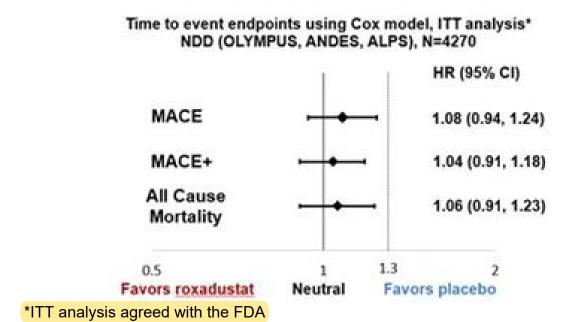
Across these pooled safety analyses, the studies evaluated several different patient populations, including:

- Non-Dialysis Dependent (NDD) patients;
- Dialysis Dependent (DD) patients; and
 - Incident Dialysis (ID) patients, who are patients who recently initiated dialysis (within 4 months). This ID subpopulation is the appropriate setting for comparison of roxadustat versus epoetin alfa, as this period of initial dialysis treatment is associated with substantially increased levels of safety events and patient mortality; whereas the stable DD patients have survived this period and thus are responsive to stable doses of erythropoiesis stimulating agents (ESA) such as epoetin alfa.

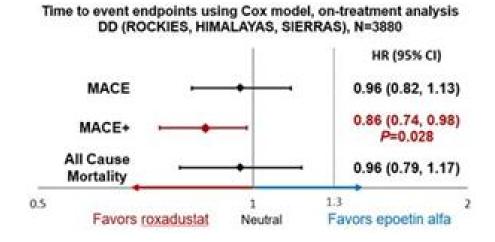
Cardiovascular (CV) endpoints were defined as:

- Time to first Major Adverse Cardiovascular Event (MACE): a composite endpoint of all-cause mortality, myocardial infarction, stroke;
- Time to first MACE+, a composite endpoint which includes MACE plus unstable angina and heart failure requiring hospitalization; and
- Time to all-cause mortality
 - In the Non-Dialysis Dependent (NDD) patient population:
 - Risks of MACE, MACE+, and all-cause mortality in roxadustat patients were comparable to placebo in the ITT analyses based on a reference non-inferiority margin

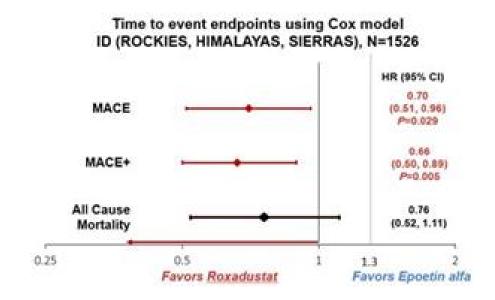
of 1.3.



- o In a post hoc subgroup analysis of 2,438 non-dialysis patients with baseline eGFR≥15,
 - The one-year decline in eGFR in roxadustat treated patients (-2.8) was significantly less than that in placebo treated patients (-4.4), with a treatment difference of 1.6 mL/min/1.73m2 (p<0.0001).
- In the Dialysis Dependent (DD) patient population:
 - Risks of MACE and all-cause mortality in roxadustat patients were not increased compared to those for patients receiving epoetin alfa based on a reference non-inferiority margin of 1.3.
 - Risk of MACE+ was 14% lower in roxadustat-treated patients than in those receiving epoetin alfa.



- The Incident Dialysis (ID) patient sub-group of the Dialysis Dependent (DD) patient population:
 - Risk of MACE was 30% lower in roxadustat patients than in epoetin alfa patients, and risk of MACE+ was 34% lower.
 - Roxadustat-treated patients' risk showed a trend towards lower all-cause mortality relative to epoetin alfa-treated patients.



"The positive efficacy and cardiovascular safety results from these pooled analyses, in a population with a broad range in both CKD and anemia severity in over 8,000 patients across six Phase 3 global trials, reaffirm the potential of roxadustat to improve treatment for anemia in CKD patients." said K. Peony Yu, MD, Chief Medical Officer, FibroGen. "There has not been much progress in treatment approaches for anemia in over 30 years, and more effective, safe, and convenient treatment options for patients are long overdue. We are privileged to be advancing this effort with roxadustat and plan to file the NDA in the U.S. by the end of this quarter for both dialysis and non-dialysis patients with our partner AstraZeneca and the MAA in Europe by the end of first quarter 2020 with our partner Astellas, followed by submissions to other regulatory authorities."

About Anemia Associated with CKD

Anemia can be a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, a protein in red blood cells that carries oxygen to cells throughout the body. Anemia in CKD is associated with increased risk of hospitalization, cardiovascular complications and death, also frequently causing significant fatigue, cognitive dysfunction and reduced quality of life. Severe anemia is common in patients with CKD, cancer, myelodysplastic syndromes (MDS), inflammatory diseases, and other serious illnesses.

Anemia is particularly prevalent in patients with CKD. The prevalence of CKD in the adult population is estimated at 10-12% globally and is generally a progressive disease characterized by gradual loss of kidney function that may eventually lead to kidney failure, or end stage renal disease, requiring

dialysis or kidney transplant to survive. Blood transfusion is used for treating life-threatening severe anemia. However, blood transfusions reduce the patient's opportunity for kidney transplant, increase risk of infections and the risk of complications such as heart failure and allergic reactions.

According to the United States Renal Data System (USRDS), over 14% of the U.S. adult population is affected by CKD, and a majority of dialysis-eligible CKD patients are currently on dialysis. It is estimated that approximately 509,000 patients are receiving dialysis in the U.S. as of 2016.

About Roxadustat

Roxadustat (FG-4592) is a first-in-class, orally administered small molecule HIF-PH inhibitor that promotes erythropoiesis through increasing endogenous production of erythropoietin, improving iron regulation, and overcoming the negative impact of inflammation on hemoglobin syntheses and red blood cell production by downregulating hepcidin. Administration of roxadustat has been shown to induce coordinated erythropoiesis, increasing red blood cell count while maintaining plasma erythropoietin levels within or near normal physiologic range in multiple subpopulations of chronic kidney disease (CKD) patients, including in the presence of inflammation and without a need for supplemental intravenous iron. Roxadustat is currently approved in China for the treatment of anemia in CKD patients on dialysis and patients not on dialysis and approved in Japan for the treatment of anemia in CKD patients on dialysis. Roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes (MDS), and in a Phase 2 U.S. trial for treatment of chemotherapyinduced anemia.

Astellas and FibroGen are collaborating on the development and commercialization of roxadustat for the treatment of anemia in territories including Japan, Europe, the Commonwealth of Independent States, the Middle East, and South Africa. AstraZeneca and FibroGen are collaborating on the development and commercialization of roxadustat for the treatment of anemia in the U.S., China, and other markets in the Americas and in Australia/New Zealand as well as Southeast Asia.

About FibroGen

FibroGen, Inc., headquartered in San Francisco, California, with subsidiary offices in Beijing and Shanghai, People's Republic of China, is a leading biopharmaceutical company discovering and developing a pipeline of first-in-class therapeutics. The company applies its pioneering expertise in hypoxia-inducible factor (HIF) and connective tissue growth factor (CTGF) biology, and clinical development to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer. Roxadustat, the company's most advanced product candidate, is an oral small molecule inhibitor of HIF prolyl hydroxylase (HIF-PH) activity, completing worldwide Phase 3 clinical development for the treatment of anemia in chronic kidney disease (CKD), is approved by the National Medical Products Administration (NMPA) in China for CKD patients on dialysis and not on dialysis and by the Ministry of Health, Labour and Welfare in Japan for CKD patients on dialysis. Roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes (MDS), and in a Phase 2 U.S. trial for treatment of chemotherapy-induced anemia. Pamrevlumab, an anti-CTGF human monoclonal antibody, is in Phase 3 clinical development for the treatment of idiopathic pulmonary fibrosis (IPF)

and pancreatic cancer, and is currently in a Phase 2 trial for Duchenne muscular dystrophy (DMD). FibroGen is also developing a biosynthetic cornea in China. For more information, please visit www.fibrogen.com.

Forward-Looking Statements

This release contains forward-looking statements regarding our strategy, future plans and prospects, including statements regarding the development of roxadustat, our interpretation of the pooled safety analyses and other analyses of the global Phase 3 program for roxadustat, , the potential for and timing of an NDA submission to the FDA and an MAA submission to the EMA for potential marketing approval for roxadustat, the potential safety and efficacy profile of our product candidates, aspects of roxadustat that could affect its commercial prospects, and our clinical, regulatory plans, and those of our partners. These forward-looking statements include, but are not limited to, statements about our plans, objectives, representations and contentions and are not historical facts and typically are identified by use of terms such as "may," "will", "should," "on track," "could," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential," "continue" and similar words, although some forward-looking statements are expressed differently. Our actual results may differ materially from those indicated in these forward-looking statements due to risks and uncertainties related to the continued progress and timing of our various programs, including the enrollment and results from ongoing and potential future clinical trials, and other matters that are described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, and our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2019 filed with the Securities and Exchange Commission (SEC), including the risk factors set forth therein. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and we undertake no obligation to update any forward-looking statement in this press release, except as required by law.

Contact:

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Investors:

Michael Tung, M.D. Investor Relations 1.415.978.1433 ir@fibrogen.com

Photos accompanying this announcement are available at

https://www.globenewswire.com/NewsRoom/AttachmentNg/42940076-9101-4178-8cee-ac4a9f974ecb

 $\underline{https://www.globenewswire.com/NewsRoom/AttachmentNg/11e33b31-2f3d-4905-8960-a5f165353fae}$

https://www.globenewswire.com/NewsRoom/AttachmentNg/89c53228-2d1d-43e1-9433-52ee642a4ff9



Source: FibroGen, Inc

EXHIBIT Q

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Roxadustat Phase III programme pooled analyses showed positive efficacy and no increased cardiovascular risk in patients with anaemia from chronic kidney disease

PUBLISHED 8 November 2019

In non dialysis-dependent patients receiving roxadustat, the risk of MACE, MACE+ and all-cause mortality was comparable to placebo

Dialysis-dependent patients receiving roxadustat had a lower risk of MACE+ and no increased risk of MACE or all-cause mortality versus epoetin alfa

In incident dialysis patients, roxadustat had a lower risk of MACE and MACE+ and showed a trend towards lower risk of all-cause mortality relative to epoetin alfa

AstraZeneca and FibroGen Inc. (FibroGen) today presented pooled efficacy and cardiovascular (CV) safety analyses from the pivotal Phase III programme assessing roxadustat for the treatment of patients with anaemia from chronic kidney disease (CKD).

The pooled CV safety analyses showed that roxadustat, an oral first-in-class hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), did not increase the risk of MACE, MACE+ and allcause mortality in non dialysis-dependent (NDD) patients compared to placebo and dialysisdependent (DD) patients compared to epoetin alfa, a current medicine used to treat anaemia.

In a clinically important predefined subgroup of incident dialysis (ID) patients, defined as patients who have been on dialysis for four months or less, roxadustat reduced the risk of MACE and MACE+ and showed a trend towards lower risk of all-cause mortality relative to epoetin alfa.

Key safety endpoints consisted of time to major adverse CV events (MACE), defined as all-cause mortality, stroke and myocardial infarction, and time to MACE+, defined as MACE, unstable angina requiring hospitalisation and congestive heart failure requiring hospitalisation.

The results were presented in an oral late-breaking abstract session at the American Society of Nephrology (ASN) Kidney Week 2019 in Washington, D.C., US.

Mene Pangalos, Executive Vice President, BioPharmaceuticals, R&D, said: "These highly anticipated results reinforce our confidence in the potential of roxadustat to address significant unmet medical needs among patients with anaemia from chronic kidney disease, particularly for those who have recently started dialysis. The pooled analyses showed incident dialysis patients receiving roxadustat had a lower risk of cardiovascular events which is important as these patients may experience higher rates of morbidity and mortality than those on stable dialysis."

Robert Provenzano, MD, Associate Professor of Medicine, Wayne State University, Detroit, Michigan, US and a primary investigator on the global Phase III programme, said: "Roxadustat is the first in a new class of medicines for the treatment of anaemia from chronic kidney disease. This pooled cardiovascular safety data, together with strong efficacy data, support its potential as an important new treatment option for patients with anaemia from chronic kidney disease who have seen little to no innovation in decades."

Key headline data from the roxadustat Phase III programme pooled safety analyses

Population Comparator	MACE	IVI A C. F. +	All-cause mortality	Conclusion
NDD (n=4,270)	(95% CI,	(95% CI,	(95% CI, 0.91, 1.23)	The risk of MACE, MACE+ and all-cause mortality in roxadustat patients was
Placebo				comparable to placebo

Population Comparator	MACE	MACE+	All-cause mortality	Conclusion
ID ^{i,ii} (n=1,526) Epoetin alfa	HR 0.70 (95% CI, 0.51, 0.96)	HR 0.66 (95% CI, 0.50, 0.89)	HR 0.76 (95% CI, 0.52, 1.11)	In ID patients, those taking roxadustat had a 30% lower risk of MACE and 34% lower risk of MACE+ compared to those taking epoetin alfa, with a trend towards lower all-cause mortality for roxadustat relative to epoetin alfa
DD (n=3,880) Epoetin alfa	HR 0.96 (95% CI, 0.82, 1.13)	HR 0.86 (95% CI, 0.74, 0.98)	HR 0.96 (95% CI, 0.79, 1.17)	No increased risk of MACE and all-cause mortality and a lower risk of MACE+ compared to epoetin alfa

- i. ID patients are those who initiated dialysis within four months prior to randomisation
- ii. ID patients are a subgroup of the DD patient population

The primary efficacy endpoint was achieved in the pooled analyses for NDD and DD patients, and in all individual Phase III trials. Data from the pooled efficacy and CV safety analyses, together with other statistical analyses, will form part of the regulatory submission in the US, which is anticipated in Q4 2019.

The pooled efficacy analyses in the NDD population showed roxadustat was superior to placebo, regardless of iron-repletion, with a mean increase from baseline in haemoglobin (Hb) levels averaged over weeks 28 to 52 of 1.85 g/dL in patients treated with roxadustat compared to 0.13 g/dL with placebo (p<0.001).

The pooled efficacy analyses in the DD population showed roxadustat demonstrated a statistically significant mean increase from baseline in Hb levels averaged over weeks 28 to 52 with 1.22 g/dL in patients treated with roxadustat compared to 0.99 g/dL with epoetin alfa (p<0.001).

Roxadustat is currently approved in China for the treatment of anaemia in patients with CKD, regardless of whether they require dialysis, and in Japan for the treatment of dialysis patients with anaemia from CKD.

About roxadustat

Roxadustat is a HIF-PHI that promotes erythropoiesis by increasing endogenous production of erythropoietin and improving iron regulation and overcoming the negative impact of inflammation on haemoglobin synthesis and red blood cell production by downregulating hepcidin. Use of roxadustat has been shown to induce coordinated erythropoiesis, increasing red blood cell count while maintaining plasma erythropoietin levels within or near normal physiologic range, in multiple subpopulations of CKD patients, including in the presence of inflammation and without a need for supplemental IV iron.

About the Phase III programme

FibroGen, Inc., (FibroGen) and AstraZeneca are collaborating on the development and commercialisation of roxadustat for the treatment of anaemia in patients with CKD in the US, China, and other global markets. FibroGen and Astellas Pharma Inc. (Astellas) are collaborating on the development and commercialisation of roxadustat for the treatment of anaemia in patients with chronic kidney disease (CKD) in territories including Japan, Europe, the Commonwealth of Independent States, the Middle East, and South Africa.

The global Phase III programme includes more than 9,000 patients and was conducted by AstraZeneca, FibroGen and Astellas together. The OLYMPUS, ALPS and ANDES trials evaluated roxadustat vs. placebo in NDD patients. ROCKIES, SIERRAS and HIMALAYAS evaluated roxadustat vs. epoetin alfa in DD patients. HIMALAYAS evaluated roxadustat vs. epoetin alfa in ID patients; there were ID patients in ROCKIES and SIERRAS. PYRENEES was not included in the pooled CV safety analyses.

About anaemia

Anaemia can be a serious medical condition in which patients have insufficient red blood cells and low levels of haemoglobin, a protein in red blood cells that carries oxygen to cells throughout the body. 1,2 Anaemia from CKD is associated with increased risk of hospitalisation, CV complications and death, also frequently causing significant fatigue, cognitive dysfunction and decreased quality of life. 4 Severe anaemia is common in patients with CKD, cancer, myelodysplastic syndrome, inflammatory diseases and other serious illnesses.

Anaemia is particularly prevalent in patients with CKD. CKD affects more than 200 million patients worldwide and is generally a progressive disease characterised by gradual loss of kidney function that may eventually lead to kidney failure.

According to the United States Renal Data System, about 80% of the approximately 509,000 patients receiving dialysis in the US in 2016 were being treated with erythropoiesis-stimulating agents (ESA).⁵ Patients seldom receive ESA treatment until they initiate dialysis therapy.

About AstraZeneca in CVRM

Cardiovascular, Renal & Metabolism (CVRM) together forms one of AstraZeneca's three therapy areas and is a key growth driver for the Company. By following the science to understand more clearly the underlying links between the heart, kidneys and pancreas, AstraZeneca is investing in a portfolio of medicines to protect organs and improve outcomes by slowing disease progression, reducing risks and tackling co-morbidities. The Company's ambition is to modify or halt the natural course of CVRM diseases and potentially regenerate organs and restore function, by continuing to deliver transformative science that improves treatment practices and cardiovascular health for millions of patients worldwide.

About AstraZeneca

AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, CVRM, and Respiratory. AstraZeneca operates in over 100 countries, and its innovative medicines are used by millions of patients worldwide. For more information, please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

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Adrian Kemp Company Secretary AstraZeneca PLC

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EXHIBIT R

S&P Global Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN FQ3 2019 Earnings Call Transcripts

Monday, November 11, 2019 10:00 PM GMT

S&P Global Market Intelligence Estimates

	-FQ3 2019-			-FQ4 2019-	-FY 2019-	-FY 2020-
	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS	CONSENSUS	CONSENSUS
EPS Normalized	(0.57)	(0.57)	NM	(0.56)	(0.34)	(0.52)
Revenue (mm)	31.61	33.17	▲ 4.94	38.69	285.77	323.51

Currency: USD

Consensus as of Nov-11-2019 11:30 AM GMT

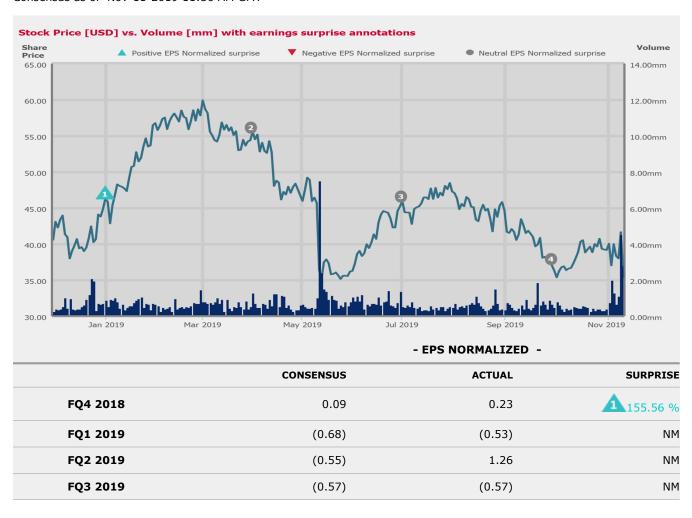


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Call Participants

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Presentation

Operator

Welcome to the FibroGen Third Quarter 2019 Financial Results Conference Call. My name is Erin, and I'll be your operator for today's call.

[Operator Instructions] Please note that this conference is being recorded. I will now turn the call over to Michael Tung. Michael, you may begin.

Michael Tung

Investor Relations Executive

Thank you, Erin, and good afternoon, everyone. Thank you for joining our call. Today, we'll be reporting financial results and corporate updates for the third quarter of 2019. Joining me today on the call are Jim Schoeneck, Interim Chief Executive Officer; Dr. Peony Yu, Chief Medical Officer; Ms. Chris Chung, Senior Vice President, China; Dr. Elias Kouchakji, Senior Vice President, Clinical Development and Drug Safety and Pharmacovigilance; and Mr. Pat Cotroneo, Chief Financial Officer.

Following our prepared remarks, Jim will discuss upcoming milestones, and we will then open the call to Q&A. During this call, we may make forward-looking statements regarding our business, including our collaborations with AstraZeneca and Astellas; financial guidance; the initiation, enrollment, design, conduct and result of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities and certain other business matters.

For risks and uncertainties regarding our business and statements made on the call today as well as factors beyond our control that may cause differences between current expectations and actual results. We refer you to our annual report on Form 10-K for the fiscal year ended December 31, 2018, and to our quarterly report on Form 10-Q for the quarter ended September 30, 2019, filed with the Securities and Exchange Commission.

Copies of these filings may be found in the Investors section of our website. We undertake no obligation to update any forward-looking statement, whether as a result of new information, future development or otherwise. The format for today's call includes remarks from FibroGen's management team, and then we'll open the lines to take your questions. The press release reporting our financial results and business update and a webcast of today's conference call can be found on the Investors section of the FibroGen website at www.fibrogen.com.

The webcast will be available for 30 days from today's date. And with that, I'd now like to turn the call over to our Interim CEO, Jim Schoeneck.

James A. Schoeneck

Chairman of the Board

Thank you, Mike, and thank you all for joining us today. During today's call, I will give you an overview of our third quarter results and recent accomplishments. Dr. Peony Yu will then give a review of the roxadustat data from the American Society of Nephrology Meeting, which just wrapped up yesterday. Following that, Chris Chung will update you on our China efforts. Dr. Elias Kouchakji will give a pamrevlumab update, and Pat Cotroneo will discuss our financials. Then I'll provide some closing comments and open the call to questions.

First, I want to take a moment to acknowledge with a great sense of loss the recent and unexpected passing of FibroGen's Founder and long-term Chairman and CEO, Tom Neff. Tom was a man of vision, determination and leadership and was deeply committed to innovation. We at FibroGen are deeply indebted to him. Tom founded FibroGen in 1993, with the vision of treating fibrosis at a time when there was no hope for the disease category. He led the company for over 25 years and established a culture and a team driven to support his vision, motivated by his commitment to improve the lives of those suffering from conditions with no satisfactory therapeutic options.

In founding FibroGen, Tom assembled global scientific leaders in areas critical to the understanding of fibrosis and the fibrotic disease mechanism, ultimately providing the basis for pamrevlumab and through the exploration of prolyl hydroxylase enzyme activity, the basis for roxadustat. Tom was intimately involved in the discovery and development of roxadustat and pamrevlumab and positioned the company for great success, given the breadth of the application for both compounds. His contribution as a pioneer in the biotechnology industry will be measured by the lives that he has and will continue to touch as FibroGen continues to develop medicines for unmet medical needs. The FibroGen Board and Management team are committed to fulfill and build upon Tom's vision.

As you all saw last month, the 2019 Nobel Prize in physiology [or] medicine was awarded to 3 physician scientists for their research into how cells send oxygen and how they function in low oxygen conditions or hypoxia. The collective contributions of Dr. Bill Kaelin of the Dana-Farber Cancer Institute; Sir Peter Ratcliffe of the University of Oxford; and Dr. Gregg Semenza of Johns Hopkins University School of Medicine identified the pathway by which cells detect oxygen and respond to hypoxia. This seminal science has paved the way for promising new strategies to fight anemia, cancer and many other diseases.

FibroGen is fortunate to work closely with Bill Kaelin, a collaborator and member of the company's scientific advisory board for nearly 2 decades. Today, roxadustat is the first medication in the world which applies this groundbreaking science. As Dr. Bob Provenzano stated at the American Society Nephrology last week, this is a great example of cutting-edge science moving from bench to bedside. Roxadustat has already approved in China for the treatment of anemia associated with chronic kidney disease, and in Japan for CKD patients on dialysis. We're also currently preparing regulatory submissions for the U.S. and Europe.

Last week, during the American Society of Nephrology Kidney Week 2019, FibroGen and our partners Astellas and AstraZeneca presented roxadustat data from our Phase III program as well as pooled cardiovascular safety and efficacy results. The pooled data kicked off ASN's high-impact clinical trial session with a packed room of almost 2,000 people. One nephrologist called it the largest crowd for an anemia presentation in well over a decade. This set of global studies covered the spectrum of chronic kidney disease, anemia, and it's believed to be the largest and most comprehensive study population ever reported with over 8,000 patients. Details of the data presented can be found on our website and in our press release from last Friday. Our studies assess cardiovascular safety and dialysis and nondialysis-dependent patients using the endpoints of major adverse cardiovascular events, known as MACE and MACE+, which adds hospitalization due to unstable angina and congestive heart failure. The pooled results show that roxadustat's cardiovascular safety was comparable to placebo in nondialysis-dependent patients. And in dialysis-dependent patients, roxadustat did not increase the risk of MACE and reduce the risk of MACE+ compared to epoetin alfa, the leading product currently used to treat this population.

Finally, in the subgroup of dialysis patients who recently started dialysis, referred to as incident dialysis patients, roxadustat reduced MACE by 30% and MACE+ by 34% compared to epoetin alfa. Roxadustat achieved the primary hemoglobin efficacy endpoints in all of these groups.

Of note, roxadustat was shown to raise hemoglobin levels regardless of iron status at baseline in patients who required no supplementary IV iron and in patients with inflammation, a group that is difficult to treat with current therapies. Having an oral product with this safety and efficacy profile can offer patients with anemia or chronic kidney disease and their doctors a treatment unlike anything currently on the market in the U.S. or Europe.

Let me briefly mention a few other highlights from the quarter. We initiated our Phase III pamrevlumab program, enrolling the first patients in our idiopathic pulmonary fibrosis or IPF trial as well as our study in locally advanced pancreatic cancer. Our Phase II IPF trial was published in the Lancet Respiratory Medicine journal and in accompanying editorial, Professor Athol Wells of the Royal Brompton Hospital stated, "In conclusion, it's difficult to imagine more encouraging Phase II results of a novel drug for IPF."

In China, we booked our first roxadustat product revenue anywhere in the world and we continue to prepare for the full market launch with our 50-50 partner, AstraZeneca. In September, FibroGen and roxadustat won the 2019 Dushu Lake Prize for innovative drug with the highest clinical value in China. I think you'll agree with me, it's been a very, very accomplished guarter.

Now I'll turn it over to Peony, who will give you a more in-depth discussion of roxadustat and the data from the ASN Meeting.

K. Peony Yu

Chief Medical Officer

Thank you, Jim. Last week, FibroGen and our partners presented roxadustat Phase III results at the Annual American Society of Nephrology Meeting, which included over 13,000 kidney professionals. As the nephrologists share our excitement of a potential game changer in anemia therapy based on strong scientific foundation. Today, I would like to review the highlights.

The pooled analyses included data from 6 Phase III trials, including over 8,000 patients and encompass over 13,000 patient exposure years. Our studies evaluated 3 patient populations; nondialysis-dependent, dialysis-dependent and incident dialysis, which is a subgroup of patients recently started dialysis within 4 months of [studies] participation. We reported on results of the following safety endpoints; major adverse cardiovascular events or MACE endpoints consists of death due to all causes, nonfatal myocardial infarction and nonfatal stroke; MACE+ consists of the 3 MACE events plus hospitalization due to heart failure or unstable angina, all-cause mortality is simply all death due to any cause.

To maintain objectivity and consistency, the events in these cardiovascular endpoints were adjudicated by independent adjudicators blinded to treatment assignment. The time-to-event analyses are conducted based on pooling strategy and analytical approaches agreed with the FDA and the time to MACE is the primary safety endpoint in the U.S., supported by results of MACE+, which is recognized as an important endpoint in the nephrology community.

In nondialysis, where roxadustat was compared to placebo, which is the gold standard in safety assessment, roxadustat was comparable to placebo in MACE and MACE+ risk using a commonly applied noninferiority margin of 1.3. In dialysis patients, roxadustat reduced the risk of MACE+ by 14% compared to epoetin alfa and had no increased risk of MACE compared to EPO using a commonly applied NI margin of 1.3.

In incident dialysis, roxadustat had a 30% lower risk of MACE and a 34% lower risk of MACE+ than EPO.

Let's discuss the rest of the efficacy and safety results, starting with nondialysis. 4,270-plus CKD patients were enrolled into the 3 Phase III nondialysis studies comparing roxadusat to placebo. In these studies, we included CKD stage 3, 4 and 5 patients of whom 42% were CKD stage 5. Their anemia tends to be more severe with their more advanced chronic kidney disease, and they have been generally excluded from prior large CKD anemia studies of ESAs. Similarly, we included patients with a range of iron [scores] with 40% of study patients non-iron [replete] at baseline, and thus, they were ineligible for ESA treatment, based on the current ESA label.

Roxadustat met the primary efficacy endpoint of mean change from baseline to average hemoglobin over weeks 28 to 52, in which -- I'm sorry, in each of the 3 individual Phase III studies and in the pooled analyses in which roxadustat was superior to placebo regardless of CKD severity, regardless of severity of anemia at baseline and regardless of iron [repletion] status. Roxadustat's efficacy is accompanied by an 81% risk reduction in use of rescue treatment, which includes IV iron, ESA and transfusion and a 74% reduction in the risk of red blood cell transfusion, with p-value of 0.001, p-value less than.

Importantly, in comparison to placebo, roxadustat patients also show a slower decline in eGFR, which is a measure of kidney function. Patients with base -- in patients with baseline eGFR of 15 or higher during the first year of treatment.

The 1-year decline in eGFR in roxa patients was 2.8, which is significantly less than the decline in placebo patients of 4.4 with a treatment difference of 1.6 and p-value has been 0 in that.

This represents a 38% reduction in eGFR decline relative to placebo. Turning to cardiovascular safety. In the CKD nondialysis pool based on ITT analysis, roxadustat was comparable to placebo.

For reference, here are the hazard ratios. MACE hazard ratio of 1.08 with 95% confidence interval of 0.94 and 1.24, MACE+ has a ratio of 1.04 with confidence interval of 0.91 and 1.18, all-cause mortality has a ratio of 1.06, with confidence interval of 0.91 and 1.23.

We have received questions on the individual components of cardiovascular composite endpoint in nondialysis with the most interest in stroke.

Well, this is most likely because of the TREAT study on that darbepoetin resulted in the ESA label restriction in its use in nondialysis and dialysis patients. I want to be clear from the outset. We believe the data from the individual components of MACE and MACE+ in the roxadustat program are consistent with the results in the overall analyses. Stated another way, we believe the results in the individual components are comparable to placebo in nondialysis. This is also true for the dialysis pool. Before we dive into details, I want to remind you that the roxadustat nondialysis program was powered for assessing the MACE composite endpoint and not the individual components.

To give a sense of magnitude, in the roxadustat program, stroke represents only 10% of the MACE events in the nondialysis pool and the incidence of rate in roxadustat is comparable to placebo, which is 1.2 per 100 patient years in roxadustat versus 1.1 in placebo arm. Hazard ratio of 1.22, with 95% confidence interval of 0.80 and 1.86.

As a reminder, in the TREAT study the incident rate of stroke in darbepoetin was twice that of placebo, with hazard ratio of 1.92 and 95% confidence interval of 1.38 and 2.18. The rest of the MACE+ component in our nondialysis pool is as follows. All-cause mortality has a ratio of 1.06, confidence interval of 0.91 and 1.23, which we stated earlier. MI has a ratio of 1.28, confidence interval of 0.9 and 1.84 and stable angina requiring hospitalization with hazard ratio of 0.49 and confidence interval of 0.19 and 1.27. Finally, congestive heart failure requiring hospitalization, which is important in CKD patients has hazard ratio of 0.89, confidence interval of 0.72 and 1.12.

Based on the composite endpoints of time to MACE, MACE+, all-cause mortality and the individual components, the overall cardiovascular safety of roxadustat is comparable to placebo. The dialysis-dependent patient pool consists of 180 patients who were randomized one-to-one to receive roxadustat or epoetin alfa in 3 dialysis Phase III studies. The primary efficacy endpoint of mean change in hemoglobin from baseline to week 28 to 52 was met in each individual study and in the pooled analyses. Roxadustat achieved higher hemoglobin level than active comparator of epoetin alfa. This result was seen in patients with or without inflammation as measured by CRP with similar roxadustat dose requirements regardless of inflammation status with roxadustat treated patients receiving less IV iron than EPO patients. While transferrin saturation or TSAT, a measure of iron store in the body were comparable between the 2 treatment arms.

In addition, when compared with EPO, roxadustat-treated patients had a lower red blood cell transfusion risk than EPO-treated patients. Hazard ratio of 0.82, p-value of 0.046.

The combination of findings above reflects the benefits of coordinated erythropoiesis with roxadustat as treatment resulted in more efficient iron utilization, lower transfusion requirement and can potentially overcome ESA hyporesponsiveness.

Turning to cardiovascular endpoint analysis of the dialysis pool. In MACE and in all-cause mortality, roxadustat had no increased risk relative to EPO.

In MACE+, roxadustat had a 14% reduction in risk compared to EPO. I would like to point out the incidence rate of each of the individual MACE+ components in dialysis are numerically lower in roxadustat than EPO.

Finally, let's talk about the exciting patient population, incident dialysis, which is a pre-specified subgroup of the dialysis-dependent pool. Here, we studied 1,526 new dialysis patients who commenced treatment within 4 months before study participation and were treated up to 3 years with an average treatment duration of 1.5 years.

In the incident dialysis pool, in comparison to epoetin alfa, roxadustat treatment resulted in a 30% reduction in the risk of MACE and a 34% reduction in the risk of MACE+ [would trend] for lower risk of death. These results suggest potential long-term safety benefits in selecting roxadustat when initiating anemia therapy in dialysis patients.

To evaluate the merits of roxadustat, it is important to put together an overall picture, taking into account efficacy and safety and ask if this drug has the potential to improve anemia treatment in CKD patients. Our answer is, yes.

In nondialysis, our Phase III program show roxadustat treatment corrected anemia effectively regardless of iron repletion and reduced risk of large scale use of blood transfusion while also slowing down the decline in kidney function in patients with EGFR greater than or equal to 15, while MACE, MACE+ and all-cause mortality risk were comparable to placebo, the gold standard.

Because of the safety-related treatment restriction of ESA, coupled with the iron repletion requirement and the inconvenience of parenteral administration requirements, currently there is little use of ESA in nondialysis patients, as USRDS reported that only 15% of patients entering dialysis had received prior ESA treatment. If approved, roxadusat could deliver the therapeutic benefits with the convenience of a pill, unlike ESA, which requires frequent injections at the doctor's office. In addition to the favorable efficacy and safety characteristics, the convenient dosing of oral medication and removal of the financial and time burden from patients need to [stock] and inject the medicine, we believe roxadustat has the potential to improve treatment access and patient compliance. Therefore, we believe we have an unprecedented opportunity to expand anemia therapy to the millions of nondialysis patients whose anemia go unaddressed.

In dialysis, currently, the decision on the choice of anemia agent is generally made at the early periods of dialysis treatment. With a 30% reduction in MACE risk and a 34% reduction in MACE+ risk compared with epoetin alfa in incident dialysis patients, we believe roxadustat could be viewed as a safer option for patients initiating chronic dialysis, while benefiting from the robust efficacy in patients with or without inflammation with less IV iron use and lower transfusion rate compared to EPO in the dialysis patients.

We are privileged to have an opportunity to potentially introduce a new standard for anemia therapy for CKD patients with roxadustat, a first-in-class agent based on Nobel winning science. We believe these compelling efficacy results with demonstration of clinical benefits accompanied by the above safety results could serve as strong basis for marketing approval in both the U.S., Europe and other countries in the world. Working with our partner, AstraZeneca, we have made a substantial progress in preparing NDA for CKD anemia in patients on dialysis and in patients not on dialysis. We plan to submit the NDA for both indications before year-end. We are working closely with Astellas, our European partner and expect to file the MAA for both indications in the first quarter of 2020.

Encouraged by the safety and efficacy results in CKD, we continue to expand treatment of anemia of other etiologies. In MDS, we have 2 ongoing clinical studies; a Phase III U.S. global study in transfusion-dependent MDS patients and a Phase II/III study in nontransfusion-dependent MDS patients in China. From Phase III global study results of the open-label [lead-in portion] , demonstrating roxadustat efficacy in MDS patients will be presented in an oral session of the upcoming American Society of Hematology Meeting in Orlando next month. We have also started a Phase II U.S. study of roxadustat for treating chemotherapy-induced anemia which we believe [to] have much opportunity to address the unmet need of a large patient population.

Our founding CEO led pioneering HIF-PHI for anemia therapy. We are committed to carry on Tom Neff's legacy to develop innovative medicines to improve patient care.

I now like to turn the call over to Chris Chung.

Christine L. Chung

Senior Vice President of China Operations

Thanks, Peony. It has been an eventful quarter for us in China. Publication of data from the 2 China-only Phase III studies in the New England Journal of Medicine was a landmark event, which was celebrated

in China with much enthusiasm. The Chinese nephrology community envisions itself as leading the way internationally in the adoption of a transformative new paradigm for the treatment of anemia in CKD.

With the expansion of the China label to include nondialysis, our partnership with AstraZeneca is serving us well. We are able to leverage the significant commercialization capability and launch experience of what is now the largest multinational pharma in China, with coverage at over 6,000 hospitals that represent the vast majority of the potential market for roxadustat. FibroGen in China has responsibility for medical affairs, and we, too, have expanded our key opinion leader coverage and evidence generation activities over the last few years from the original 30 Phase III clinical trial sites to now over 300 leading hospitals and counting.

As a joint team, we continue to advance our efforts in market development, distribution, reimbursement and gaining listings in hospitals. China, as the first launch market for roxadustat, has given us some very encouraging early signals about prescriber and patient receptivity, indicators which are helping us calibrate the scale and scope of our ambitions for the market. Looking at the different segments of the potential patient universe.

In dialysis, the installed base of over 600,000 patients is now the single -- the largest single country dialysis population of the world, exceeding that of the United States. This is a substitution market for roxadustat. Treatment of anemia is well established, but only 1/5 of patients are treated to the target hemoglobin [of 11] . There continues to be double-digit growth in dialysis. After accounting for deaths, nearly 100,000 new patients come on to dialysis each year. They represent new candidates for roxadustat, and many have no prior ESA experience.

Within dialysis is approximately 100,000 patients or 14% who are treated on peritoneal dialysis, PD instead of hemodialysis, HD. We believe this segment is particularly well suited for an oral therapeutic like roxadustat because patients receive PD treatment at home. Finally, the nondialysis segment is even bigger in patient count, but ESA use is much less established. We believe, as an oral therapy, roxadustat has the opportunity to greatly expand the addressable market. We expect to know by the end of 2019 if roxadustat will be included in the updated National Reimbursement Drug List or NRDL. Inclusion would be an important inflection point for the business as it would greatly increase patient affordability, accelerate hospital listings and expand overall market adoption. This remains a stretch goal as historically, the NRDL cycles were farther part in time and drugs were on the market for a few years before inclusion.

In the event roxadustat is not admitted in this round, reimbursement would be a top priority for us in 2020. We look forward to keeping you updated on the exciting market opportunity in front of us in China.

With this, I'll turn it over to Elias to describe [this] development in pamrevlumab.

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Thank you, Chris, and good afternoon. I'd like to start with introduction of pamrevlumab. It is the first-in-class fully human monoclonal antibody that inhibit the activity of connected tissue growth factors, also known as CTGF. It's a critical mediators of the progression of fibrosis in fibroproliferative diseases.

Pamrevlumab is currently in Phase III clinical development for the treatment of both idiopathic pulmonary fibrosis, IPF, and unresectable locally advanced pancreatic cancer, also known as LAPC. Pamrevlumab is in the Phase II for the treatment of the Duchenne muscular dystrophy in nonambulatory patients. These diseases share a commonality of fibrosis involvement, and each represent an area of significant unmet medical needs in which these patients face a dire prognosis.

I would like to start with an update on IPF. In July, we dosed the first patient in the ZEPHYRUS Phase III clinical study of pamrevlumab in patients with IPF. We continue to activate additional sites in this study and engage with our investigators to enroll patients. We are redoubling our efforts in improving our processes to bring sites online and expect an acceleration over the next few months. Our focus now is to activate sites with the expectation that the enrollment will accelerate in the year of 2020. In September, as Jim mentioned, we announced The Lancet Respiratory Medicine Publication of positive results from the company's PRAISE Phase II clinical study in IPF, showing both significant improvement in the primary

efficacy endpoint of FVC change from baseline and reduction in disease progression in quantitative lung fibrosis as measured by HRCT, also known as high-resolution CT scan.

This paper was well received by the medical community at the 2019 European Respiratory Society International Congress. We are very appreciative and encouraged by this reception. In this publication, the authors reported that pamrevlumab demonstrated the potential for stabilization of disease and for the first time in human studies, the potential reversal of lung fibrosis in some patients.

I'd like to remind everyone that pamrevlumab has received Orphan Drug and Fast Track designation from the FDA for the treatment of IPF.

Moving to LAPC. Our Phase II results showed encouraging clinical evidence of potential of pamrevlumab plus chemotherapy to transform unresectable LAPC patient into patients who are eligible for surgical resection. We recently announced that the first patient was dosed in LAPIS our pivotal Phase III randomized, double-blind, placebo-controlled study, evaluating pamrevlumab as a new adjuvant therapy for unresectable LAPC patients. This study will enroll 260 patients approximately, to receive chemotherapy of gemcitabine and nab-paclitaxel and will be randomized to either pamrevlumab or placebo.

As you may know, this is a very sick patient with limited options. With a primary endpoint of overall survival, at the end of the treatment period, we will be evaluating the rate of resection as a surrogate endpoint for a potential accelerated approval. Similar to IPF, pamrevlumab have received both Orphan Drug and Fast Track designation from the FDA for the treatment of this disease.

Turning to the Duchenne muscular dystrophy, we will meet with the FDA this quarter to discuss the design of our pivotal Phase III program in DMD. We look forward to updating you in the future as this program advances. Also, we plan in the near future to publish additional data from patients who have completed 1 year of treatment in our Phase II study. Pamrevlumab has received Orphan Drug Designation from the FDA for the treatment of DMD.

In clinical study, in multiple indications, pamrevlumab has consistently shown positive efficacy results, has demonstrated a good safety and tolerability profile. We are pleased to be progressing with the Phase III studies.

To fulfill the vision of our late CEO, Tom Neff, whose goal in founding FibroGen was to treat fibrotic diseases. We look forward to updating you on the progress of the pamrevlumab program in the future.

I will turn now the call to our CFO, Pat Cotroneo for the financial update. Pat?

Pat Cotroneo

Senior VP of Finance & CFO

Thank you, Elias. As announced today, total revenue for the quarter ended September 30, 2019, was \$33.2 million as compared to \$29 million for the third quarter of 2018. For the same period, operating costs and expenses were \$86 million and net loss was \$49.4 million or \$0.57 per basic and diluted share as compared to operating costs and expenses of \$71.8 million and a net loss of \$42.6 million or \$0.50 per basic and diluted share for the third quarter last year. Included in revenue for the quarter ended September 30, 2019, are first commercial sales of roxadustat drug product in China. The related net product revenue was \$600,000 for the quarter. Also, included in operating costs and expenses for the quarter ended September 30, 2019, was an aggregate noncash portion totaling \$19.6 million, of which \$14.8 million was a result of stock-based compensation expense as compared to an aggregate noncash portion of \$16 million, of which \$14.3 million was a result of stock-based compensation expense for the same period in the prior year.

As stated in Q2 2019, in accordance with the U.S. GAAP, we have included our revenue recognition methodology, a total of \$180 million comprised of \$50 million for an anticipated milestone from AstraZeneca relating to the filing of the U.S. NDA and \$130 million in anticipated milestones from Astellas in connection with the EU MAA filings when such milestone achievements became probable. Included in our third quarter revenue recognition methodology is a \$12.5 million milestone associated with the approval for CKD in dialysis patients in Japan. The timing of when the payments related to these

milestones will be remitted to FibroGen depends when the milestones are actually achieved. As noted earlier on this call, our NDA submission is targeted for Q4 this year and we expect the Astellas MAA submission to occur in the second half of the Astellas 2019 fiscal year, which ends at March 31, 2020. Based on our latest forecast, we estimate our 2019 ending cash to be in the range of \$650 million to \$660 million, and this range includes the \$50 million U.S. NDA milestone.

At September 30, 2019, FibroGen had \$666.5 million in cash, restricted time deposits, cash equivalents, investments and receivables.

Thank you. And I would now like to turn the call back over to Jim.

James A. Schoeneck

Chairman of the Board

As you have heard, we've made significant progress over the past few months. Looking forward, we will continue to drive our products, programs and organization. Here are some of our areas of focus: first, FibroGen's board and our Search Committee has initiated a search to find a truly exceptional leader to be FibroGen's permanent CEO. We'll update you as we have more news of our selection.

For pamrevlumab, we're enrolling our Phase III studies for both IPF and locally advanced pancreatic cancer and will focus on opening additional study sites and increasing patient enrollment. We also look forward to discussions with the FDA to determine the next steps in our Duchenne Muscular Dystrophy program.

In China, our focus is on securing reimbursement and the upcoming roxadustat launch. We look forward to updating you on that progress in the coming months as well. For roxadustat, we are completing our NDA submission in conjunction with AstraZeneca and plan to file by the end of this quarter, followed by the European MAA submission through our partner Astellas by March of 2020.

As Pat mentioned, FibroGen is eligible to receive \$180 million in filing milestones from our partners, and we are also eligible to receive similar scope approval milestones. Finally, we plan to submit the data just presented at the ASN for publication, and we'll continue to seek out new indications for roxadustat with our programs in MDS and CIA. At this point, I'd like to open up the call for questions.

Question and Answer

Operator

[Operator Instructions]

And your first question comes from Michael Yee.

Michael Jonathan Yee

Jefferies LLC, Research Division

Congrats on the progress. I know Tom would have been proud had he been there, and congrats on all the progress. Two questions. One is for Peony. I would just like to understand, since there seems to be some investor concern about FDA agreements and FDA sign-off [from] statistical [stance] , how your general impression was of your meeting with the FDA? And why you feel confident about statistical protocols and their signing off of what you have from statistics and why you feel good about that?

And my second question is for Jim. In your seat, although I appreciate you're the interim CEO, perhaps you could talk about what your priorities are and what the Board's priorities are at this point given where the stock is at, where things are, I guess what you're thinking about in terms of priorities from here. I appreciate it.

K. Peony Yu

Chief Medical Officer

Mike, thank you for the [good] question. First of all, I wanted to share that we have been in dialogue with the FDA in the past 6 years. And there has been a very good understanding about what the Phase III required study would look like and including the size of the study, how to power it [for example] what's the primary endpoint and we agree on time to meet at the primary endpoint, and that's how we power for the non-dialysis and the dialysis. And we've also had a very productive dialogue with the FDA on the analysis of cardiovascular safety as well as what the efficacy requirement needs to be for this submission. And the most recent conversation with the FDA was at the end of July. And we had sent it to the FDA, a fairly comprehensive briefing package and had a very productive meeting. And walking out of it, we felt that we had all the guidance from the FDA we needed to put together a winning submission. And that is about to be out the door this quarter.

Michael Jonathan Yee

Jefferies LLC, Research Division

So you feel no issue or no real concern about the hazard ratios and the [upper bounds] and all the things that people are talking about? You look at diabetes programs and things like that, there's -- you're well within that. So you don't feel any concern about that?

K. Peony Yu

Chief Medical Officer

No, we have no concern about that. And Mike, as you know, that our regulatory assessment is not based on 1 criterion. But instead, it is based on totality of evidence such as efficacy, safety, what is the medical need. And so based on our discussions and the historical precedents in this therapeutic area and the various conversations we've had with the agency, we are very comfortable with our data where it is now.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. And Jim, just that question for you.

James A. Schoeneck

Chairman of the Board

And Mike, I think our focus is very clear as I mentioned through the -- my closing remarks, I mean first and foremost, it's filing of the NDA; second, it's filing through Astellas, the MAA in Europe. Behind that is China, and they're securing reimbursement, along with the support and our participation in the China launch. And with pamrevlumab, it's around accelerating both the number of sites and the enrollment in our 2 Phase III studies and getting agreement with the FDA on where we're taking the DMD program next. I think beyond that, working with the rest of the board, it's finding a very capable person to step in and lead the company longer term.

Operator

And your next question comes from Geoffrey Porges.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

I just wanted to also share my sadness and sympathy about Tom and particularly important that given all the recognition and the progress that you've made with roxadustat and pamrevlumab. So 1 question for Peony, if I may, one Chris -- question for Chris. Peony, could you share the number of patients in the non-dialysis cohorts that progressed [to] dialysis and the difference in timing in the progression of dialysis and perhaps comment about whether the patient's post progression of dialysis, presumably were treated with EPO and behaved in the same way as the incident dialysis patients. And so was there a benefit from the comparison between roxa and EPO in relation to progressed?

And then Chris, could you talk a little bit more about the NRDL listings, specifically have you applied for both dialysis and non-dialysis? And what is the size of the non-dialysis patient population who are anemic enough to justify treatment with innovative drugs such as roxa?

K. Peony Yu

Chief Medical Officer

Geoff, you asked a lot of this -- I noticed that the question was more than one. So I think that it is correct to expect that when 40% of the -- all of the non-dialysis patient pool were indeed already -- had already reached end-stage kidney disease, meaning eGFR being below 15, then you do expect some patients to require dialysis treatment in this long-term outcome program. And so we are -- now the analysis of these patients is important because transition -- that represents a transition to dialysis. And we have not had a chance. As you see, we have presented a lot of data at the ASN. We have not had a chance to write this one up yet, and we agree with you, this is important that we should present in future medical conferences or publications. It's a little bit complicated to report that at a Q&A at -- over here.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

[indiscernible] Was there a benefit in time?

K. Peony Yu

Chief Medical Officer

I'm sorry?

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Was there a benefit at least in time? Was there a significant difference in the time to progress to dialysis between the 2 cohorts?

K. Peony Yu

Chief Medical Officer

Based on the results from the eGFR change, we believe there should be, but the data needs to -- needs further analysis as mainly because the time on treatment between roxadustat and placebo differ.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. Chris, I'd love to hear from you about NRDL.

Christine L. Chung

Senior Vice President of China Operations

Hi, Geoff. So your first question, I believe, is whether roxadustat was invited by the Chinese government to NRDL negotiations.

So first of all, you're absolutely right. A sponsor is invited. You don't proactively apply. So I think consistent with what AstraZeneca, our partners, have said, the 2 companies are collectively putting a lot of effort in getting into NRDL. At this point in time, we're not discussing if there's an invitation primarily because all invitations either to roxadustat or to other companies are considered confidential. And the Chinese government has not published a list of companies invited to negotiate. So I would prefer to wait until the end of the year when the outcomes in NRDL is disclosed. I hope you understand.

With regard to the second question, I believe the question was, what is the size -- potential market size of non-dialysis. So I had mentioned just now in my section of the script that there are over 600,000 dialysis patients in China, 90% to 95% of them are anemic. In non-dialysis, if you look at the CKD population, it's actually 120 million, of course mostly, they are early stage, and they're not necessarily anemic. If you look at Stage IIIb, it's about 50%; Stage IV, about 70%; Stage V, non-dialysis is about 90%. If you add those numbers up based on the real world evidence data that we have, measurement hemoglobin 10 and below, we believe the addressable market in China for non-dialysis anemic patients below hemoglobin 8 is close to 2 million patients. It's a substantial population. And Geoff, we're very excited because we have an oral therapeutic with a safety profile that we think would greatly expand the addressable market.

Operator

And your next question comes from Adam Walsh.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

This is Edwin on for Adam. First question maybe for Peony. For the individual MACE component in the NDD, I guess the events for myocardial infarction and stroke in that data set [have more] , and FDA will focus on the MACE composite. Can you please further clarify on this NDD MACE data set?

K. Peonv Yu

Chief Medical Officer

Yes. So I wanted to reiterate that in our conversation with the FDA, the primary safety endpoint was the composite MACE, and there was never any requirement stated for us to -- for -- on the individual component itself. And I also, again, remind ourselves that these numbers are fairly -- the number of events are fairly small. And that -- now another thing to point out is that the lower bound of the 95% confidence intervals on each of these individual components are below 1.0, which is very different than the [stroke in treat] . And we are looking at the overall picture and the overall safety profile of the drug looking at efficacy, safety as well as what -- how little is on the market for treating the non-dialysis patients.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

Okay. My second question is when are you going to talk about the [the job] as stat plan? I mean the statistical analysis plan, including the non-inferiority margin. Is there any pre-planned FDA meeting in the coming weeks?

K. Peony Yu

Chief Medical Officer

I am sorry about the questions. Are you asking when we will publish these results? We do plan to write it up as soon as we can and put it in a scientific journal.

James A. Schoeneck

Chairman of the Board

I think -- Adam (sic) [Edwin], I think is -- the question is when will we talk to the FDA about the statistics and the analytical plan is the question.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

Right.

James A. Schoeneck

Chairman of the Board

We plan to talk to them in the coming weeks.

K. Peony Yu

Chief Medical Officer

Okay. So the answer to that question is that we had already talked with the FDA about analytical plan, and we had made the agreement on the analysis plan. The results that we have presented in the high-impact clinical session at the ASN, and the numbers I had just presented were based on the agreed analysis plan that we have made with the FDA.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

So the noninferiority margin of [1.3] is already in agreement or not?

K. Peony Yu

Chief Medical Officer

So we are talking about the analysis plan, meaning how do you pool, what's the pooling strategy and the analysis plan, how to analyze the data. When you talk about NI margins, you're talking about the standard for assessment, right? And as I mentioned earlier, that we expect that [all] regulators will assess the data based on the very -- all the -- on the entire application of the NDA. And based on our dialogue with FDA over the past 6 years and the data, as we have shown, we are confident that we do have what it takes for this drug to be favorably evaluated.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

All right. Maybe another question for Chris, regarding the China market. Can you help us understand more of the self-pay market there? And how do you and AstraZeneca book revenue and cost in China? Is it 50-50?

Christine L. Chung

Senior Vice President of China Operations

So Edwin with regard to the first question about the self-pay market, so the self-pay market is not large. And this is why getting into NRDL, it's an important inflection point for the business. The self-pay market is basically people not getting reimbursement and choosing to pay 100% out-of-pocket at a price, and it's visible to the market for a roxadustat drug that is higher than the standard of care. We have sales at this point in time, so there is a self-pay market, but we do not expect it to be substantial because of the differential in pricing.

With regard to revenue recognition, FibroGen is the marketing authorization holder of roxadustat in China. And under the 2 invoices role, it is the manufacturing -- it's the marketing authorization holder that books

revenues. We have a 50-50 profit share with AstraZeneca. So that is how the 50-50 works. It's not a 50-50 split of the top line, it's the 50-50 split of the profits.

Operator

And your next question comes from Danielle Brill.

Nirav Y. Shelat

Piper Sandler & Co., Research Division

Congratulations on the data. I just had a couple of questions. This is Nirav on for Danielle, by the way. I was just wondering, would you be able to talk a little about whether you're expecting priority review or a normal review with the NDA? And if you'd be willing to use a priority review voucher?

K. Peony Yu

Chief Medical Officer

This is a very good question. And we believe that the basis for a priority review could be because we have a new innovative drug that is potentially better than what is available for treating diseases in patients with a serious condition. However, the decision whether to grant us priority review is [that one] of the FDA.

James A. Schoeneck

Chairman of the Board

So Nirav, your -- the second part of your question, I would not see us using a priority review voucher, but we will and request priority review.

Nirav Y. Shelat

Piper Sandler & Co., Research Division

Okay, I see. That's helpful. And I guess my second question would be, would you be able to give us just some color on the MDS study? Just how it's going, how the enrollment is going and when we should expect data? And along with other agents that are currently in the pipeline for the indication as well, how do you see roxadustat sort of [fitting] in from a strategic standpoint?

K. Peony Yu

Chief Medical Officer

Good question. We do -- we are seeing encouraging data from the open-label portion of our Phase III study, which is what we will be presenting in the upcoming ASH. And since the other -- so in terms of the competitive landscape, we believe that because MDS is such a -- MDS anemia is a condition that there is so much need and so difficult to treat, we believe that there is still opportunity for us to make a difference in these patients. And the enrollment is ongoing. And we will come back with a -- in the future, the time line on when the study will be completed.

Operator

And your next question comes from Paul Choi.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

My first question is for Peony. And you did state earlier that the non-dialysis population was not powered to individually assess the various components of MACE. But given the background of the patient population in terms of their eGFR level, can you give us -- what is your understanding with regard to the FDA's position on the individual components with respect to when a trial is not powered to show a statistical difference on those individual points, given the patient's background population? And then I had a second commercial question on the NRDL.

K. Peony Yu

Chief Medical Officer

So to -- we can share our view on the individual components and what's the discussion with the FDA in terms of the requirement for our primary safety endpoint. And as I stated earlier, there was never any explicit expectation on the individual components. Now -- but we do believe that the evaluation of the data has to take into account the overall benefit risk of the drug for the patient. So I hope this answer the question.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Yes. And then on the NRDL, I know you stated you haven't -- you won't formally communicate whether roxadustat is under invitation to be considered. But assuming it is under consideration, I guess, as you think about potential reference pricing in the competitive landscape, given the wide availability of EPO in China, can you maybe give us what you think of reasonable range is potentially for pricing on the goforward given the availability and pricing of EPO in the China market?

Christine L. Chung

Senior Vice President of China Operations

Absolutely, Paul. So the way we think about pricing in China is as follows. So first of all, as value-based pricing, we evaluate the scope of unmet medical need and the pharmacoeconomic consequences of not treating or not treating optimally or not treating safely. We then compared the clinical efficacy benefits of roxadustat based on the China Phase III studies over ESAs, and then we looked at the safety advantages over ESAs. And this is all about differentiation on a clinical basis. We also, with AstraZeneca, believe that roxadustat as a first-in-class drug and a patented first-in-class drug, of course, to state the obvious, deserves an innovation premium because we are bringing a transformative new treatment paradigm to China, that above and beyond the clinical benefit to the patient in a quantifiable unmet medical need, also supports the country's policy direction of encouraging innovation. So we're hopeful that roxadustat could become an example of company bringing innovation to China and expecting a return for that delivery. We do not see ourselves being benchmarked against locally manufactured ESA because we think we're a highly differentiated product with clinical benefits, and we believe we deserve an innovation premium.

Obviously, Paul, at the end of the day, it's about budgetary concerns and budgetary considerations of the Chinese government and affordability for the patient. So at the end of the day, should there be an NRDL negotiations, pricing would not just be what we would like to assert but what the country can actually afford. So we'd be eager to see what that balance is should there be an NRDL negotiation, but that is our pricing strategy in terms of what we believe is a fair pricing for roxadustat.

Operator

And your next question comes from Mr. Joel Beatty.

Joel Lawrence Beatty

Citigroup Inc, Research Division

All right. Great. So the -- my first question is on the quality of life benefit from the Phase III program. I believe that there was some initial data presented in the top line data, but then I didn't see anything on quality of life at ASN. Should we still consider the quality of life effect to be in line with the top line press release? And how important will low quality of life data from the Phase III program be for marketing the drug?

K. Peony Yu

Chief Medical Officer

Joe, it is great questions. Yes, our data is consistent with what we had reported in top line. And we just have so much to put together for the ASN, and we do look forward to present the results in future conferences and publications. As you know, one of the manifestations of anemia is -- for patients is fatigue and largely, quality of life. Thank you.

Joel Lawrence Beatty

Citigroup Inc, Research Division

Great. And then maybe one other question. Can you tell us about the indication you plan to pursue for roxadustat?

K. Peony Yu

Chief Medical Officer

Yes. So we and our partners believe that roxadustat has the potential to become the anemia drug for various kinds of anemia beyond CKD. And as we have presented, we already have ongoing trial in MDS anemia and in chemotherapy-induced anemia. And there are additional anemia types that are in consideration, such as anemia in multiple myeloma patients and anemia of inflammation. There has been extensive effort to evaluate all these types of anemia and more.

Operator

And there are no questions at this time.

James A. Schoeneck

Chairman of the Board

Well, in closing, I'd like to thank you for your attention and support. I also want to thank the senior management team and all of the dedicated employees at FibroGen in the U.S. and in China, who are committed to bringing novel innovative medicines to patients around the world, fulfilling the vision that Tom set for the company 25 years ago. Thank you.

Operator

Thank you, ladies and gentlemen. This concludes today's conference. Thank you for participating. You may now disconnect.

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EXHIBIT S

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-Q

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☑ QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the quarterly period ended September 30, 2019

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to Commission file number: 001-36740

FIBROGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)
409 Illinois Street
San Francisco, CA
(Address of Principal Executive Offices)

77-0357827 (I.R.S. Employer Identification No.)

> 94158 (Zip Code)

(415) 978-1200

Registrant's telephone number, including area code:

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which			
		registered			
Common Stock, \$0.01 par value	FGEN	The Nasdaq Global Select Market			

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes \square No \square

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (\S 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes \square No \square

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer	✓	Accelerated filer	
Non-accelerated filer		Smaller reporting company	
		Emerging growth company	

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. \Box

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2). Yes □ No ☑

The number of shares of common stock outstanding as of October 31, 2019 was 87,250,064.

FIBROGEN, INC.

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8. Related Party Transactions

Astellas is an equity investor in the Company and considered a related party. The Company recorded revenue related to collaboration agreements with Astellas of \$15.5 million and \$5.1 million for the three months ended September 30, 2019 and 2018, respectively, and \$155.0 million and \$30.8 million for the nine months ended September 30, 2019 and 2018, respectively.

The Company recorded expense related to collaboration agreements with Astellas of \$0.9 million and \$0.4 million during the three months ended September 30, 2019 and 2018, respectively, and \$2.2 million and \$1.1 million during the nine months ended September 30, 2019 and 2018.

As of September 30, 2019 and December 31, 2018, accounts receivable from Astellas were \$17.7 million and \$47.2 million, respectively, and amounts due to Astellas were \$1.7 million and \$0.4 million, respectively. The accounts receivable from Astellas as of September 30, 2019 included \$12.5 million of the milestone payment the Japan Agreement related to Japan's NDA approval by the Ministry of Health, Labour and Welfare for the treatment of anemia associated with CKD in dialysis patients. The accounts receivable from Astellas as of December 31, 2018 included \$43.8 million related to the delivery of roxadustat active pharmaceutical ingredients to Astellas during the fourth quarter of 2018, pursuant to an amendment to the Japan Agreement that will allow Astellas to manufacture roxadustat drug product for commercialization in Japan. This amount was received during the first quarter of 2019.

Prepaid expenses and other current assets as of September 30, 2019 included \$126.0 million of net unbilled contract asset, representing a \$130.0 million unbilled contract asset related to two regulatory milestones under the Europe Agreement with Astellas associated with the planned MAA submission to the EMA, net of \$4.0 million of associated deferred revenue. See Note 2 for details. According to the Europe Agreement, this \$130.0 million is not billable to Astellas until the submission of an MAA, therefore the net contract asset was included in the prepaid expenses and other current assets line on the Company's condensed consolidated balance sheet as of September 30, 2019. There was no such contract asset balance as of December 31, 2018.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q, and in our Securities and Exchange Commission ("SEC") filings, including our Annual Report on Form 10-K for the year ended December 31, 2018 filed with the SEC on February 27, 2019.

FORWARD-LOOKING STATEMENTS

The following discussion and information contained elsewhere in this Quarterly Report on Form 10-Q contain "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended ("Exchange Act"), Section 27A of the Securities Act of 1933, as amended ("Securities Act") and within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "estimate," or "continue," and similar expressions or variations. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section titled "Risk Factors," set forth in Part II, Item 1A of this Quarterly Report on Form 10-Q. The forward-looking statements in this Quarterly Report on Form 10-Q represent our views as of the date of this Quarterly Report on Form 10-Q. We anticipate that subsequent events and developments will cause our views to change. New risks emerge from time to time, and it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this Quarterly Report on Form 10-Q may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. While we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Quarterly Report on Form 10-Q and are cautioned not to place undue reliance on such forward-looking statements.

BUSINESS OVERVIEW

We were incorporated in 1993 in Delaware and are headquartered in San Francisco, California, with subsidiary offices in Beijing and Shanghai, People's Republic of China ("China"). We are a leading biopharmaceutical company discovering and developing a pipeline of first-in-class therapeutics. We apply our pioneering expertise in hypoxia-inducible factor ("HIF"), connective tissue growth factor ("CTGF") biology, and clinical development to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer. Roxadustat, our most advanced product, is an oral small molecule inhibitor of HIF prolyl hydroxylase ("HIF-PH") activity, completing Phase 3 clinical development for the treatment of anemia in chronic kidney disease ("CKD"), with a New Drug Application ("NDA") now approved in China in dialysis patients and non-dialysis patients and in Japan for dialysis patients. We and our collaboration partners AstraZeneca AB ("AstraZeneca") and Astellas Pharma Inc. ("Astellas") are in the process of preparing an NDA for submission to the United States ("U.S.") Food and Drug Administration ("FDA") and a Marketing Authorization Application ("MAA") for submission to the European Medicines Agency ("EMA"). Roxadustat is in Phase 3 clinical development in China for anemia associated with myelodysplastic syndromes ("MDS"). Roxadustat is in Phase 2 clinical development for chemotherapy-induced anemia. Pamrevlumab, an anti-CTGF human monoclonal antibody, is in Phase 3 clinical development for the treatment of both idiopathic pulmonary fibrosis ("IPF") and pancreatic cancer. Pamrevlumab is also currently in a Phase 2 trial for Duchenne muscular dystrophy ("DMD"). We are also developing a biosynthetic cornea in China.

Financial Highlights

	T	Three Months Ended September 30,			Nine Months Ended September 30,			
	2019		2018		2019			2018
			((in thousands, except	for per share data)			
Result of Operations								
Revenue	\$	33,174	\$	29,027	\$	248,603	\$	104,903
Operating costs and expenses	\$	86,028	\$	71,799	\$	237,481	\$	211,516
Net income (loss)	\$	(49,439)	\$	(42,556)	\$	21,153	\$	(107,373)
Net income (loss) per share - basic	\$	(0.57)	\$	(0.50)	\$	0.24	\$	(1.28)
Net income (loss) per share - diluted	\$	(0.57)	\$	(0.50)	\$	0.23	\$	(1.28)
					Se	ptember 30, 2019	De	ecember 31, 2018
						(in tho	usano	ds)
Balance Sheet								
Cash and cash equivalents					\$	196,592	\$	89,258
Short-term and long-term investments					\$	443,039	\$	587,964
Accounts receivable					\$	19,225	\$	63,684

Our revenue for the three and nine months ended September 30, 2019 increased compared to the same periods a year ago. Our revenue for the three and nine months ended September 30, 2019 included the recognition substantially all of \$12.5 million of a regulatory milestone that was included in the transaction price during the third quarter of 2019 when this milestone was achieved. This milestone is associated with the NDA approval in Japan under the collaboration agreement with Astellas for roxadustat as the treatment for dialysis CKD patients. In addition, our revenue for the nine months ended September 30, 2019 included of the recognition of \$129.0 million of two regulatory milestones totaling \$130.0 million that were included in the transaction price during the second quarter of 2019 when these milestones became probable of being achieved. These milestones are associated with the planned MAA submission to the EMA under the collaboration agreement with Astellas for roxadustat as a treatment for dialysis and non-dialysis CKD patients. Our revenue recognized during the nine months ended September 30, 2019 also included the recognition of \$42.1 million of a \$50.0 million regulatory milestone that was included in the transaction price during the second quarter of 2019 when this milestone became probable of being achieved. This milestone is associated with the planned NDA submission to the FDA under the collaboration agreement with AstraZeneca for roxadustat as a treatment for dialysis and non-dialysis CKD patients. As comparison, our revenue for the prior year period included the recognition of \$14.9 million of a \$15.0 million regulatory milestone associated with NDA submission in Japan under the collaboration agreement with Astellas for roxadustat for the treatment of anemia in Japan that was included in the transaction price during the second quarter of 2018 when this milestone became probable of being achieved. The increases were partially offset by a decrease in co-development billings related to the development

Operating costs and expenses for the three months ended September 30, 2019 increased compared to the same period a year ago primarily due to \$20.2 million higher outside service expenses related to co-promotional activities and scientific contract expenses, \$2.6 million amortization of finance lease right-of-use ("ROU") assets related to the adoption of lease accounting guidance under Accounting Standards Codification ("ASC") 842 - Leases ("ASC 842"), \$1.6 million higher depreciation expenses mainly due to the change in estimated useful life for our leasehold improvements as a result of the adoption of ASC 842, and \$1.4 million higher legal expenses mainly associated with patent-related and international activities. The increases were partially offset by \$5.5 million lower drug development expenses associated with drug substance manufacturing activities related to pamrevlumab, \$4.7 million lower clinical trial expenses related to lower activities for roxadustat offset by higher activities for pamrevlumab, and \$3.7 million capitalization of inventory manufacturing costs.

Operating costs and expenses for the nine months ended September 30, 2019 increased compared to the same period a year ago primarily due to \$31.7 million higher outside service expenses related to co-promotional activities and scientific contract expenses, \$10.4 million higher stock-based compensation related to the cumulative impact of stock option grant activities, \$7.8 million amortization of finance lease ROU assets related to the adoption of lease accounting guidance under ASC 842, \$3.9 million higher depreciation expenses mainly due to the change in estimated useful life for our leasehold improvements as a result of the adoption of ASC 842, \$2.9 million higher legal expenses mainly associated with patent-related and international activities, and \$2.4 million higher employee-related expenses resulting from higher average compensation level. The increases were partially offset by \$16.4 million lower clinical trial expenses related to lower activities for roxadustat offset by higher activities for pamrevlumab, \$11.7 million lower drug development expenses associated with drug substance manufacturing activities related to pamrevlumab, and \$4.3 million capitalization of inventory manufacturing costs.

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During the three months ended September 30, 2019, we had a net loss of \$49.4 million, or net loss per basic and diluted share of \$0.57, as compared to a net loss of \$42.6 million for the same period a year ago, due to an increase in operating costs and expenses partially offset by an increase in revenue. During the nine months ended September 30, 2019, we had a net income of \$21.2 million, or net income per basic share of \$0.24, and net income per diluted share of \$0.23, as compared to a net loss of \$107.4 million for the same period a year ago, due to an increase in revenue partially offset by an increase in operating costs and expenses.

Cash and cash equivalents, investments and accounts receivable totaled \$658.9 million at September 30, 2019, a decrease of \$82.0 million from December 31, 2018, primarily due to the cash used in operations, partially offset by the accounts receivable at December 31, 2018 collected during the year.

Research, Development and Commercial Programs

Roxadustat for the Treatment of Anemia in Chronic Kidney Disease

Roxadustat is our most advanced product, an oral small molecule inhibitor of HIF-PH activity that acts by stimulating the body's natural pathway of erythropoiesis, or red blood cell production. In August 2019, roxadustat (China tradename: 爱瑞卓®) received marketing authorization in China for the treatment of anemia caused by CKD in non-dialysis patients (adding non-dialysis to the label for dialysis which was approved in 2018). In September 2019, roxadustat (Japan tradename Evrenzo®) was approved in Japan for the treatment of anemia associated with CKD in dialysis patients.

We have reported top line efficacy data from individual studies from the roxadustat Phase 3 trials in December 2018, and top line pooled cardiovascular safety data in May 2019. We recently reported additional individual study data and pooled safety data at the American Society of Nephrology Kidney Week 2019. We expect these data will serve as the basis to submit the roxadustat U.S. NDA in the fourth quarter of 2019 for CKD anemia in both dialysis and non-dialysis patients, followed by the MAA in Europe in the first quarter of 2020.

· Pooled Efficacy Data

In addition to meeting the U.S. primary efficacy endpoint in each of six individual Phase 3 studies, roxadustat superiority over placebo was demonstrated in the primary endpoint as the mean change in hemoglobin (from baseline to the average between weeks 28-52) was significantly larger than placebo (1.85 g/dL vs. 0.13 g/dL, p<0.001) in the non-dialysis pool (4,277 patients from OLYMPUS, ANDES, and ALPS). In addition, the mean change in hemoglobin (from baseline to the average between weeks 28-52) in roxadustat patients was significantly larger than in epoetin alfa patients (1.22 g/dL vs. 0.99 g/dL, p<0.001) in the pooled dialysis studies (3,857 patients from HIMALAYAS, SIERRAS, and ROCKIES).

o Patients with Inflammation

In a subgroup of dialysis patients with inflammation (C-reactive protein ("CRP") levels over 4.9 mg/L), the mean change in hemoglobin (from baseline to the average between weeks 28-52) was significantly higher in roxadustat-treated patients (1.29 g/dL) than epoetin alfa treated patients (0.96 g/dL, p<0.0001).

o Intravenous ("IV") Iron Requirement; Efficacy Irrespective of Iron Replete Status

In non-dialysis, roxadustat increased hemoglobin (by 1.94 g/dL) regardless of whether patients were iron-replete (patients shown to have sufficient baseline stores of iron in their body, TSAT \geq 20% and Ferritin \geq 100 ng/mL) or not iron-replete. In dialysis, less mean monthly IV iron supplementation was required at weeks 28-52 in patients receiving roxadustat versus patients receiving epoetin alfa in pooled analysis, p< 0.0001.

o Risk of Rescue Therapy and Transfusion

The risk of rescue therapy was significantly lower in the roxadustat arm (8.9%) than the placebo arm (31.1%) in the pooled non-dialysis patients with a hazard ratio ("HR") = 0.19 (95% confidence interval "95% CI" of 0.16, 0.23), p<0.0001. The percentage of patients receiving red blood cell transfusions during the first year of treatment was also significantly lower in the roxadustat arm (5.2%) as compared to the placebo arm (15.4%) (HR (95% CI) = 0.26 (0.21, 0.32), p<0.0001).

In the dialysis pool, during the first year of treatment, patients in the roxadustat arm had a lower transfusion risk (9.5%) as compared to the epoetin alfa arm (12.8%) (HR (95% CI) = 0.82 (0.679, 0.997), p=0.046).

o Reduction of Decline in Kidney Function as Measured by eGFR

In a post hoc subgroup analysis of 2,438 non-dialysis patients with baseline eGFR≥15, the one-year decline in estimated glomerular filtration rate ("eGFR," a measure of the filtration function of kidney and renal disease progression) in roxadustat treated patients (-2.8) was significantly less than that in placebo treated patients (-4.4), with a treatment difference of 1.6 mL/min/1.73m² (p<0.0001).

o Reduction of LDL Cholesterol

In the pooled non-dialysis patients, roxadustat lowered low-density lipoproteins ("LDL"), with a mean change from baseline of -17.06 mg/dL compared to an increase of 1.30 mg/dL for placebo patients, a significant treatment difference of -19.83 mg/dL (p<0.0001).

• Pooled Cardiovascular Safety Data

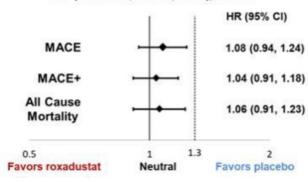
In the U.S., the primary safety endpoint is time to first Major Adverse Cardiovascular Event ("MACE"), a composite endpoint of all-cause mortality, stroke and myocardial infarction. In Europe, the primary safety endpoint is the time to first MACE+ ("MACE+") which, in addition to the components in MACE, also includes hospitalization due to heart failure or unstable angina. However, the FDA in the U.S., and the EMA in Europe, will each review MACE, MACE+, and all-cause mortality separately, in addition to other endpoints.

The below cardiovascular safety analyses reflect the pooling strategy and analytical approach we agreed on with the FDA. Similar sets of analyses will be submitted to the EMA to serve as the basis for potential approval in dialysis and non-dialysis in Europe, and additional supportive analyses and sensitivity analyses as well as subgroup analyses will also be included in the NDA and MAA. However, the FDA and EMA will each conduct their own benefit-risk analysis and may use additional statistical analyses other than those agreed with the FDA or set forth below, including, but not limited to, pre-specified or other analyses that may not sufficiently address the differential drop-out rate between the roxadustat and placebo study arms in non-dialysis.

o Non-Dialysis - Pooled Cardiovascular Safety Data

In our pre-NDA meeting, the FDA agreed that the ITT-analysis would be our primary cardiovascular safety analysis method for non-dialysis in the U.S. as it uses on-treatment and post treatment long term follow-up (until a common study end date) to account for the higher drop-out rate in the placebo arm. The figure below shows that in the 4,270 pooled non-dialysis patients (OLYMPUS, ANDES, and ALPS), the risk of MACE, MACE+, and all-cause mortality in roxadustat patients were comparable to that in placebo patients based on a reference non-inferiority margin of 1.3.

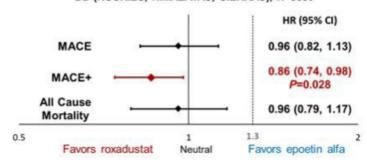




o Dialysis - Pooled Cardiovascular Safety Data

In the pooled analysis of 3,880 dialysis patients (HIMALAYAS, SIERRAS, and ROCKIES), the risk of MACE and all-cause mortality in roxadustat patients were not increased, and roxadustat lowered the risk of MACE+ by 14% compared to the active comparator epoetin alfa, based on a hazard ratio of 0.86 and an upper bound of 95% CI under 1.0. The hazard ratios represent a point estimate of relative risk.

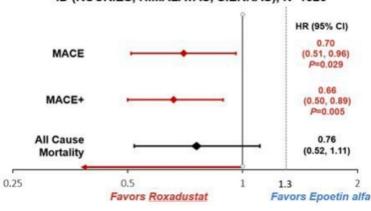
Time to event endpoints using Cox model DD (ROCKIES, HIMALAYAS, SIERRAS), N=3880



o Incident Dialysis Subgroup

In the clinically important subgroup of 1,526 incident dialysis patients, roxadustat reduced the risk of MACE by 30% and MACE+ by 34%, with a trend towards lower all-cause mortality. The lower MACE and MACE+ risks (compared to epoetin alfa) are based on hazard ratios of 0.70 and 0.66, respectively, with the upper bound of 95% CI under 1.0 in both. We believe this incident dialysis subpopulation is the appropriate setting for comparison of roxadustat versus epoetin alfa as anemia therapy often starts early in dialysis treatment, and this period of initial dialysis treatment has substantially increased patient mortality, whereas the stable dialysis population have survived this period and are already shown to be responsive to stable ESA doses.





Data from Individual Studies Presented at ASN

We and our partners also presented data from our individual Phase 3 roxadustat studies at the American Society of Nephrology Kidney Week 2019.

O Non-Dialysis CKD Patients (ANDES) - FibroGen

ANDES is a 922-patient Phase 3, randomized, double-blinded, placebo-controlled trial designed to evaluate the efficacy and safety of roxadustat vs. placebo for the treatment of anemia in patients with later stage CKD (stages 3, 4 or 5) who are not dialysis dependent.

U.S. primary efficacy endpoint: roxadustat was superior to placebo in mean hemoglobin change from baseline to the average over weeks 28 to 52 (2.00 vs. 0.16 g/dL, respectively, p<0.0001).

EU primary efficacy endpoint: a higher proportion of roxadustat-treated patients (86.0%) achieved a hemoglobin response (defined as achieving a hemoglobin level of at least 11 g/dL on two consecutive visits during the first 24-weeks of treatment and a hemoglobin increase of at least 1.0 g/dL in subjects with baseline Hb >8.0 g/dL, or an increase of at least 2.0 g/dL in subjects with baseline Hb \leq 8.0 g/dL), as compared to placebo (6.6%), p=0.0007.

The proportion of subjects who received any rescue therapy (blood/RBC transfusion, ESA use, or IV iron) in the first 52 weeks of treatment was 8.9% in the roxadustat arm vs. 28.9% in the placebo arm (HR (95% CI) = 0.19 (0.138, 0.276), p<0.0001). The proportion of subjects who received blood/RBC transfusion in the first 52 weeks of treatment was 5.6% in the roxadustat arm vs. 15.4% in the placebo arm (HR (95% CI) = 0.26 (0.165, 0.406), p<0.0001).

The mean change in LDL cholesterol from baseline to average over weeks 12-28 was -18.48 mg/dL (n=564) in the roxadustat arm vs. 0.22 mg/dL (n=269) in the placebo arm, with a treatment difference of -17.26 mg/dL (p<0.0001).

In this study, roxadustat-treated patients had a sustained reduction in hepcidin whereas placebo patients did not have a reduction in hepcidin. The mean change from baseline to week 44 was -22.1µg/L in the roxadustat arm vs. 3.88 µg/L in the placebo arm, for a treatment difference between the two arms of -25.71 µg/L (95% CI: -38.523, -12.903).

In this study, subjects in the roxadustat arm had a substantially higher overall study drug exposure compared to subjects in the placebo arm. Study drug discontinuation was higher in the placebo arm compared to roxadustat arm, and the relative difference in discontinuation rates was especially pronounced in the lowest baseline eGFR category. The overall exposure-adjusted safety profile of roxadustat observed during this study was comparable with placebo and consistent with that expected in the CKD study population. The most frequently observed adverse events with roxadustat in this trial were nausea, hyperkalemia, constipation, and hypertension.

o Incident Dialysis CKD Patients Study (HIMALAYAS) - FibroGen

HIMALAYAS is a 1,043-patient Phase 3 randomized, open-label, active-controlled trial to assess the efficacy and safety of roxadustat compared to epoetin alfa, an ESA, for the treatment of anemia in CKD patients who have newly initiated dialysis treatment for end-stage renal disease ("ESRD") and have had minimal or no exposure to an ESA prior to study participation.

U.S. primary efficacy endpoint: the mean hemoglobin change from baseline to the average over weeks 28 to 52 was 2.57 g/dL (roxadustat) vs. 2.36 g/dL (epoetin alfa), a least squares mean difference of 0.18 g/dL, with the 95% CI of (0.08, 0.29). The non-inferiority criteria was met as the lower bound of the 95% CI was well above the non-inferiority margin of -0.75 g/dL, and superiority over epoetin alfa was also achieved, p=0.0005. In subgroup analyses, roxadustat was also superior to epoetin alfa in hemoglobin change from baseline regardless of iron repletion and inflammation status.

EU primary efficacy endpoint: a higher proportion of roxadustat-treated patients (88.2%) achieved a hemoglobin response (defined as achieving a hemoglobin level of at least 11 g/dL on two consecutive visits during the first 24-weeks of treatment and a hemoglobin increase of at least 1.0 g/dL in subjects with baseline Hb \geq 8.0 g/dL), or an increase of at least 2.0 g/dL in subjects with baseline Hb \leq 8.0 g/dL), as compared to an 84.4% responder rate in the epoetin alfa arm, with the lower bound of the 95% CI (-0.7%, 7.7%) of the treatment difference in responder rate well above the non-inferiority margin of -15%.

The most frequently observed adverse events with roxadustat in this trial were hypertension, diarrhea, and muscle spasms. The safety profile of roxadustat in this study was consistent with results from prior roxadustat studies.

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o Stable Dialysis CKD Patients Study (SIERRAS) - FibroGen

SIERRAS is a 741-patient U.S. Phase 3, randomized, open-label, active-controlled trial to assess the efficacy and safety of roxadustat compared to epoetin alfa for the treatment of anemia in dialysis CKD patients who were receiving stable doses of ESA prior to study participation.

U.S. primary efficacy endpoint: the mean hemoglobin change from baseline to the average over weeks 28 to 52 was 0.39 g/dL (roxadustat) vs. -0.09 g/dL (epoetin alfa), a least squares mean treatment difference of 0.48 g/dL (95% CI 0.37, 0.59). Roxadustat met the non-inferiority criteria as the lower bound of 95% CI was well above the non-inferiority margin of -0.75 g/dL. Roxadustat also achieved superiority, p<0.0001.

EU primary efficacy endpoint: the mean hemoglobin change from baseline to the average over weeks 28 to 36 was 0.54 g/dL (roxadustat) vs. -0.03 g/dL (epoetin alfa), a least squares mean treatment difference of 0.54 g/dL with a 95% CI (0.40, 0.69). Roxadustat met the non-inferiority criteria as the lower bound of the 95% CI was well above the non-inferiority margin of -0.75 g/dL. Roxadustat also achieved superiority over epoetin alfa, p<0.0001.

In patients with inflammation (CRP>4.9 mg/L), roxadustat doses for maintaining hemoglobin levels were comparable to those with normal CRP and were stable over time as the effect on hemoglobin was durable, whereas epoetin alfa patients required higher mean doses in inflamed patients (CRP>4.9 mg/L), doses which increased by approximately 50% from baseline after about one year. In these inflamed patients (CRP>4.9 mg/L) mean change in hemoglobin from baseline to week 18-24 was 0.61 g/dL in roxadustat vs. -0.03 g/dL in the epoetin alfa group, p<0.0001.

Subjects in the roxadustat group received lower mean IV iron during weeks 28 to 52 than subjects in the epoetin alfa group (p=0.00091). Roxadustat-treated patients had a greater reduction in hepcidin as compared to ESA-treated patients. Additionally, a lower proportion of subjects on roxadustat received a red blood cell transfusion during treatment than the epoetin alfa group (12.5% and 21.1%, respectively, p=0.0337), with reduction in RBC transfusion risk by 33% compared with epoetin alfa; HR (95% CI) = 0.67 (0.466, 0.970), p=0.0337.

Mean LDL cholesterol levels decreased in the roxadustat group from baseline to the average over weeks 12 to 28 (-13.70 mg/dL) but increased in the epoetin alfa group (1.23 mg/dL) with a treatment difference of -14.67 mg/dL (p<0.0001).

The incidence of treatment emergent adverse events was comparable in the roxadustat and epoetin alfa arms and were generally consistent with those typically expected in study patient population of ESRD on chronic dialysis therapy. The most frequently observed adverse events with roxadustat in this trial were nausea, hypertension, vomiting, and hyperkalemia.

Non-Dialysis CKD Patients (OLYMPUS) - AstraZeneca

OLYMPUS is AstraZeneca's Phase 3, randomized, double-blinded, placebo-controlled trial designed to evaluate the efficacy and safety of roxadustat vs. placebo for the treatment of patients with anemia in CKD stages 3, 4 or 5 whose disease progression is moderate to severe and who are non-dialysis dependent. The trial in 2,781 patients met its primary efficacy endpoint by demonstrating a statistically-significant improvement in mean change from baseline in hemoglobin levels averaged over weeks 28 to 52 (1.75 g/dL) as compared with Placebo (0.40 g/dL).

Roxadustat also improved hemoglobin levels from baseline in a subgroup of patients with inflammation (CRP>5 mg/L), with a statistically significant mean increase of 1.73 g/dL, compared to 0.62g/dL with placebo.

Overall safety findings are generally consistent with the non-dialysis patient population. For all patients, the most frequently reported adverse events in the intent to treat analysis set were end-stage renal disease, pneumonia, urinary tract infection and hypertension.

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o Non-Dialysis CKD Patients (ALPS) - Astellas

ALPS is Astellas' Phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of roxadustat for the treatment of anemia in CKD in 597 patients not on dialysis. The trial met its primary endpoints by demonstrating superiority in efficacy vs. placebo in terms of hemoglobin change from baseline at weeks 28 to 52 (1.988 for roxadustat vs 0.406 for placebo, p<0.001).

Roxadustat was superior to placebo in its ability to lower LDL from baseline with an LS mean difference of -0.701 mmol/L (95% CI: -0.83, -0.57). Roxadustat was superior to placebo in delaying the need for rescue therapy (HR (95%CI) = 0.238 (0.17, 0.33), p<0.001).

The safety profile observed in this study was in line with the expected event profile in non-dialysis patients. Common adverse events in both treatment groups were end-stage renal disease, hypertension, peripheral edema, and decreased glomerular filtration rate.

Stable Dialysis CKD Patients (ROCKIES) - AstraZeneca

ROCKIES is AstraZeneca's Phase 3, randomized, open-label, active-controlled trial designed to assess the efficacy and safety of roxadustat vs. epoetin alfa, for the treatment of anemia in patients with CKD who are dialysis dependent. The trial in 2,133 patients met its primary efficacy endpoint by demonstrating a statistically-significant improvement in mean change from baseline in hemoglobin levels averaged over weeks 28 to 52 (0.77 g/dL) compared with epoetin alfa (0.68 g/dL).

Roxadustat also improved hemoglobin levels from baseline in a subgroup of patients with inflammation (CRP>5 mg/L, demonstrating a statistically significant improvement with a mean increase of 0.80 g/dL compared to 0.59 g/dL with epoetin alfa. Patients treated with roxadustat used less monthly IV iron (mean = 59mg) compared to those treated with epoetin alfa (mean = 91mg) from week 36 to the end of the study.

Adverse events with roxadustat were generally similar to those seen in patients treated with epoetin alfa and commonly found in dialysis patients. In roxadustat treated patients, the most frequently reported adverse events were diarrhoea, hypertension, pneumonia, headache and arteriovenous fistula thrombosis.

o Stable Dialysis CKD Patients (PYRENEES) - Astellas

PYRENEES is Astellas' Phase 3, randomized, active-controlled trial designed to assess the efficacy and safety of roxadustat vs. epoetin alfa or darbepoetin alfa, for the treatment of anemia in 838 patients with CKD who are dialysis dependent. The trial met its primary efficacy endpoint: roxadustat was considered non-inferior to ESAs based on the mean change from baseline in average hemoglobin levels at weeks 28 to 52 (0.397 vs 0.183; non-inferiority margin = -0.75).

Roxadustat was superior to ESAs in its ability to lower LDL from baseline with an LS mean difference of -0.377 mmol/L (95% CI: -0.451, -0.305). Roxadustat was superior to ESAs in reducing the need for monthly IV iron use (LS mean difference (95%CI) = -31.9 mg (-41.4, -22.4), p<0.001).

The safety profile observed in this study was in line with the expected event profile in dialysis patients. There was a greater proportion of deaths in the roxadustat treatment group compared with the ESA group; however, the study was not powered to assess risk of MACE events or death, as compared to the pooled analysis above. Common adverse events in both treatment groups were hypertension, arteriovenous fistula thrombosis, headache, and diarrhea.

Roxadustat for the Treatment of Anemia in Myelodysplastic Syndromes

In addition to anemia in CKD, we are continuing to enroll the 156-patient double-blind, placebo-controlled portion of our global Phase 3 clinical study of roxadustat in transfusion-dependent, lower risk MDS patients. The primary endpoint is the proportion of patients who achieve transfusion independence.

In China, the Phase 2/3 clinical trial to evaluate the safety and efficacy of roxadustat in non-transfusion dependent, lower risk MDS patients with anemia is ongoing. The primary endpoint for this study is percentage of patients achieving a hemoglobin response.

Roxadustat for the Treatment of Anemia in Chemotherapy-Induced Anemia

We began a Phase 2 clinical trial of roxadustat in the U.S. in chemotherapy-induced anemia in the third quarter of 2019. This is a Phase 2 single-arm open label study investigating the efficacy and safety of roxadustat for the treatment of anemia in patients receiving chemotherapy treatment for non-myeloid malignancies in the U.S., with treatment duration of 16 weeks, and will enroll up to 100 patients.

Pamrevlumab (FG-3019) - Monoclonal Antibody Against Connective Tissue Growth Factor (CTGF)

Pamrevlumab is our human monoclonal antibody that inhibits the activity of CTGF, a central mediator and critical common element in the progression of fibrotic and fibro-proliferative diseases. We initiated our Phase 3 clinical trials of pamrevlumab for the treatment of IPF and for locally advanced unresectable pancreatic cancer. We recently presented topline results from our 1-year data from our ongoing Phase 2 trial for DMD.

In the U.S., the FDA has granted Orphan Drug Designation to pamrevlumab for the treatment of IPF, locally advanced unresectable pancreatic cancer, and DMD. Pamrevlumab has also received Fast Track designation from the FDA for the treatment of both IPF and locally advanced unresectable pancreatic cancer.

Idiopathic Pulmonary Fibrosis

We recently began enrolling ZEPHYRUS and continue to enroll patients in this double-blind, placebo-controlled Phase 3 trial of pamrevlumab in approximately 565 IPF patients.

• Locally Advanced Unresectable Pancreatic Cancer

We recently began enrolling LAPIS, our double-blind placebo controlled Phase 3 trial of pamrevlumab as a neoadjuvant therapy for locally advanced unresectable pancreatic cancer. We intend to enroll approximately 260 patients, randomized 1:1 to receive either pamrevlumab in combination with gemcitabine and nab-paclitaxel, or placebo with gemcitabine and nab-paclitaxel.

Duchenne Muscular Dystrophy

In DMD, all 21 non-ambulatory patients from our fully enrolled Phase 2 open-label single-arm trial have completed over one year of treatment with pamrevlumab. Based on our administrative analysis and advice we received from expert advisors, we are planning to share these results with the FDA in the fourth quarter of this year to discuss our clinical development plan for DMD.

Collaboration Partnerships for Roxadustat

Our current and future research, development, manufacturing and commercialization efforts with respect to roxadustat and our other product candidates currently in development depend on funds from our collaboration agreements with Astellas and AstraZeneca as described below.

Astellas

In June 2005, we entered into a collaboration agreement with Astellas for the development and commercialization (but not manufacture) of roxadustat for the treatment of anemia in Japan ("Japan Agreement"). In April 2006, we entered into the Europe Agreement with Astellas for roxadustat for the treatment of anemia in Europe, the Commonwealth of Independent States, the Middle East, and South Africa. Under these agreements, we provide Astellas the right to develop and commercialize roxadustat for anemia indications in these territories.

We share responsibility with Astellas for clinical development activities required for the U.S. and the EU regulatory approval of roxadustat and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will own and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

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The Astellas agreements will continue in effect until terminated. Either party may terminate the agreements for certain material breaches by the other party. In addition, Astellas will have the right to terminate the agreements for certain specified technical product failures, upon generic sales reaching a particular threshold, upon certain regulatory actions, or upon our entering into a settlement admitting the invalidity or unenforceability of our licensed patents. Astellas may also terminate the agreements for convenience upon advance written notice to us. In the event of any termination of the agreements, Astellas will transfer and assign to us the regulatory filings for roxadustat and will assign or license to us the relevant trademarks used with the products in the Astellas territories. Under certain terminations, Astellas is also obligated to pay us a termination fee.

Consideration under these agreements includes a total of \$360.1 million in upfront and non-contingent payments, and milestone payments totaling \$557.5 million, of which \$542.5 million are development and regulatory milestones and \$15.0 million are commercial-based milestones. Total consideration, excluding development cost reimbursement and product sales-related payments, could reach \$917.6 million. The aggregate amount of such consideration received through September 30, 2019 totals \$487.6 million. Additionally, under these agreements, Astellas pays 100% of the commercialization costs in its territories. Astellas will pay us a transfer price, based on net sales, in the low 20% range for our manufacture and delivery of roxadustat.

In September 2019, Japan's Ministry of Health, Labour and Welfare approved roxadustat for the treatment of anemia associated with dialysis CKD patients. Accordingly, the consideration of \$12.5 million associated with this milestone was included in the transaction price and allocated to performance obligations under the Japan Agreement in the third quarter of 2019. This milestone payment was received in October 2019.

During the second quarter of 2019, we received positive topline results from analyses of pooled major adverse cardiac event ("MACE") and MACE+ data from its Phase 3 trials evaluating roxadustat as a treatment for dialysis and non-dialysis CKD patients, enabling Astellas to prepare for an MAA submission to the EMA during their fiscal year 2019, which ends on March 31, 2020, following our planned NDA submission to the FDA in 2019. We evaluated the two regulatory milestone payments associated with the planned MAA submission and concluded that these milestones became probable of being achieved in the second quarter of 2019. Accordingly, the total consideration of \$130.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the Europe Agreement in the second quarter of 2019

In addition, as of September 30, 2019, Astellas had separate investments of \$80.5 million in the equity of FibroGen, Inc.

AstraZeneca

In July 2013, we entered into the U.S./RoW Agreement, a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in the U.S. and all territories not previously licensed to Astellas, except China. In July 2013, through our China subsidiary and related affiliates, we entered into the China Agreement, a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in China. Under these agreements we provide AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories. We share responsibility with AstraZeneca for clinical development activities required for U.S. regulatory approval of roxadustat.

In 2015, we reached the \$116.5 million cap on our initial funding obligations (during which time we shared 50% of the joint initial development costs), therefore all development and commercialization costs for roxadustat for the treatment of anemia in CKD in the U.S., Europe, Japan and all other markets outside of China have been paid by Astellas and AstraZeneca since reaching the cap.

In China, FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") will conduct the development work for CKD anemia, will hold all of the regulatory licenses issued by China regulatory authorities, and will be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is also responsible for 100% of development expenses in all other licensed territories outside of China. Outside of China, we are responsible, through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the AstraZeneca agreements.

Under the AstraZeneca agreements, we will receive upfront and subsequent non-contingent payments totaling \$402.2 million. Potential milestone payments under the agreements total \$1.2 billion, of which \$571.0 million are development and regulatory milestones and \$652.5 million are commercial-based milestones. Total consideration under the agreements, excluding development cost reimbursement, transfer price payments, royalties and profit share, could reach \$1.6 billion. The aggregate amount of such consideration received through September 30, 2019 totals \$444.2 million.

Under the U.S./RoW Agreement, AstraZeneca will pay for all commercialization costs in the U.S. and RoW and AstraZeneca will be responsible for the U.S. commercialization of roxadustat, with FibroGen undertaking specified promotional activities in the end-stage renal disease segment in the U.S. In addition, we will receive a transfer price for delivery of commercial product based on a percentage of net sales in the low- to mid-single digit range and AstraZeneca will pay us a tiered royalty on net sales of roxadustat in the low 20% range.

Under the China Agreement, which is conducted through FibroGen China Anemia Holdings, Ltd. ("FibroGen China"), the commercial collaboration is structured as a 50/50 profit share. AstraZeneca will conduct commercialization activities in China and fund roxadustat launch costs in China until FibroGen Beijing has achieved profitability. At that time, AstraZeneca will recoup 50% of their historical launch costs out of initial roxadustat profits in China.

Payments under these agreements include over \$500.0 million in upfront, non-contingent and other payments received or expected to be received prior to the first U.S. approval, excluding development expense reimbursement.

AstraZeneca may terminate the U.S./RoW Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon 180 days prior written notice at will. If AstraZeneca terminates the U.S./RoW Agreement at will, in addition to any unpaid non-contingent payments, it will be responsible for paying for a substantial portion of the post-termination development costs under the agreed development plan until regulatory approval.

AstraZeneca may terminate the China Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon advance prior written notice at will. If AstraZeneca terminates our China Agreement at will, it will be responsible for paying for transition costs as well as make a specified payment to FibroGen China.

In the event of any termination of the agreements, but subject to modification upon termination for technical product failure, AstraZeneca will transfer and assign to us any regulatory filings and approvals for roxadustat in the affected territories that they may hold under our agreements, grant us licenses and conduct certain transition activities.

As mentioned above, during the second quarter of 2019, we received positive topline results from analyses of pooled MACE and MACE+ data from its Phase 3 trials for roxadustat, enabling our NDA submission to the FDA, which is anticipated in 2019. We evaluated the regulatory milestone payment associated with this planned NDA submission and concluded that this milestone became probable of being achieved in the second quarter of 2019. Accordingly, the consideration of \$50.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the U.S./ RoW Agreement in the second quarter of 2019.

Additional Information Related to Collaboration Agreements

Total cash consideration received through September 30, 2019 and potential cash consideration, other than development cost reimbursement, transfer price payments, royalties and profit share, pursuant to our existing collaboration agreements are as follows:

	Cash Received Through September 30,2019		Additional Potential ash Payments in thousands)	Total Potential Cash Payments		
Astellasrelated-party:						
Japan Agreement	\$	77,593	\$ 95,000	\$	172,593	
Europe Agreement		410,000	 335,000		745,000	
Total Astellas		487,593	430,000		917,593	
AstraZeneca:						
U.S. / RoW Agreement		389,000	860,000		1,249,000	
China Agreement		55,200	 321,500		376,700	
Total AstraZeneca		444,200	1,181,500		1,625,700	
Total revenue	\$	931,793	\$ 1,611,500	\$	2,543,293	

These collaboration agreements also provide for reimbursement of certain fully burdened research and development costs as well as direct out of pocket expenses.

PART II-OTHER INFORMATION

ITEM 1, LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below in addition to the other information included or incorporated by reference in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

We have marked with an asterisk (*) those risks described below that reflect substantive changes from the risks described under Part I, Item 1A "Risk Factors" included in our Annual Report on Form 10-K for the year ended December 31, 2018.

Risks Related to Our Financial Condition and History of Operating Losses

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or sustain profitability. We may require additional financings in order to fund our operations.*

We are a clinical-stage biopharmaceutical company with two lead product candidates in clinical development, roxadustat in anemia in chronic kidney disease ("CKD") and myelodysplastic syndromes ("MDS"), and pamrevlumab (FG-3019) in idiopathic pulmonary fibrosis ("IPF"), pancreatic cancer and Duchenne muscular dystrophy ("DMD"). Pharmaceutical product development is a highly risky undertaking. To date, we have focused our efforts and most of our resources on hypoxia-inducible factor ("HIF") and fibrosis biology research, as well as developing our lead product candidates. We are not profitable and, other than in 2006 and 2007 due to income received from our Astellas Pharma Inc. ("Astellas") collaboration, have incurred annual losses each year since our inception. We have not generated any revenue based on commercial drug product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss for the year ended December 31, 2018 was approximately \$86.4 million, and our net loss for the years ended December 31, 2017, and 2016, recast from amounts previously reported due to the adoption of the new revenue standards, were approximately \$120.9 million and \$58.1 million, respectively. As of September 30, 2019, we had an accumulated deficit of \$686.6 million. As of September 30, 2019, we had capital resources consisting of cash, cash equivalents and short-term investments of \$628.6 million plus \$11.0 million of long-term investments classified as available for sale securities. Despite contractual development and cost coverage commitments from our collaboration partners, AstraZeneca AB ("AstraZeneca") and Astellas, and the potential to receive milestone and other payments from these partners, and despite commercialization efforts in China and Japan for roxadustat for the treatment of anemia caused by CKD, we anticipate we will continue to incur losses on an annual basis for the foreseeable future, and we anticipate these losses will increase as we continue our development of and seek regulatory approval for our product candidates and in our commercialization efforts. If we do not successfully develop and continue to obtain regulatory approval for our existing or any future product candidates and effectively manufacture, market and sell any product candidates that are approved, we may never generate product sales, and even if we do generate product sales, we may never achieve or sustain profitability on a quarterly or annual basis. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

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We believe that we will continue to expend substantial resources for the foreseeable future as we continue late-stage clinical development of roxadustat, grow our operations in the People's Republic of China ("China"), expand our clinical development efforts on pamrevlumab, seek regulatory approval, prepare for the commercialization of our product candidates, and pursue additional indications. These expenditures will include costs associated with research and development, conducting preclinical trials and clinical trials, obtaining regulatory approvals in various jurisdictions, and manufacturing and supplying products and product candidates for ourselves and our partners. In particular, in our planned Phase 3 clinical trial program for roxadustat, which we believe will be the largest Phase 3 program ever conducted for an anemia product candidate, we are expecting to enroll more than 8,000 patients for our United States ("U.S.") and European programs alone. We are conducting this Phase 3 program in conjunction with Astellas and AstraZeneca, and we are substantially dependent on Astellas and AstraZeneca for the funding of this large program. The outcome of any clinical trial and/or regulatory approval process is highly uncertain and we are unable to fully estimate the actual costs necessary to successfully complete the development and regulatory approval process for our compounds in development and any future product candidates. We believe that the net proceeds from our 2017 public offerings, our existing cash and cash equivalents, short-term and longterm investments and accounts receivable, and expected third-party collaboration revenues will allow us to fund our operating plans through at least the next 12 months. Our operating plans or third-party collaborations may change as a result of many factors, which are discussed in more detail below, and other factors that may not currently be known to us, and we therefore may need to seek additional funds sooner than planned, through offerings of public or private securities, debt financings or other sources, such as royalty monetization or other structured financings. Such financings may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. We may also seek additional capital due to favorable market conditions or strategic considerations even if we currently believe that we have sufficient funds for our current or future operating plans.

Our future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress in the development of our product candidates;
- the costs of development efforts for our product candidates, such as pamrevlumab, that are not subject to reimbursement from our collaboration partners;
- the costs necessary to obtain regulatory approvals, if any, for our product candidates in the U.S., China and other jurisdictions, and
 the costs of post-marketing studies that could be required by regulatory authorities in jurisdictions where approval is obtained;
- the continuation of our existing collaborations and entry into new collaborations;
- the time and unreimbursed costs necessary to commercialize products in territories in which our product candidates are approved for sale:
- the revenues from any future sales of our products as well as revenue earned from profit share, royalties and milestones;
- the level of reimbursement or third-party payor pricing available to our products;
- the costs of establishing and maintaining manufacturing operations and obtaining third-party commercial supplies of our products, if any, manufactured in accordance with regulatory requirements;
- · the costs we incur in maintaining domestic and foreign operations, including operations in China;
- regulatory compliance costs;
- · the costs of our commercialization efforts for roxadustat for the treatment of anemia caused by CKD in China and Japan; and
- the costs we incur in the filing, prosecution, maintenance and defense of our extensive patent portfolio and other intellectual property rights.

Additional funds may not be available when we require them, or on terms that are acceptable to us. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations or activities that may be necessary to commercialize our product candidates.

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All of our recent revenue has been earned from collaboration partners for our product candidates under development.*

Substantially all of our revenues recognized in recent years have been from our collaboration partners.

We will require substantial additional capital to achieve our development and commercialization goals, which for our lead product, roxadustat, is currently contemplated to be provided under our existing third-party collaborations with Astellas and AstraZeneca.

If either or both of these collaborations were to be terminated, we could require significant additional capital in order to proceed with development and commercialization of our product candidates, including with respect to our expected commercialization for roxadustat for the treatment of anemia caused by CKD in China and Japan, or we may require additional partnering in order to help fund such development and commercialization. If adequate funds or partners are not available to us on a timely basis or on favorable terms, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations.

If we are unable to continue to progress our development efforts and achieve milestones under our collaboration agreements, our revenues may decrease and our activities may fail to lead to commercial products.

Substantially all of our revenues to date have been, and a significant portion of our future revenues are expected to be, derived from our existing collaboration agreements. Revenues from research and development collaborations depend upon continuation of the collaborations, reimbursement of development costs, the achievement of milestones and royalties and profits from our product sales, if any, derived from future products developed from our research. If we are unable to successfully advance the development of our product candidates or achieve milestones, revenues under our collaboration agreements will be substantially less than expected.

Risks Related to the Development and Commercialization of Our Product Candidates

We are substantially dependent on the success of our lead product, roxadustat, and our second compound in development, pamrevlumab.*

To date, we have invested a substantial portion of our efforts and financial resources in the research and development of roxadustat and pamrevlumab. While we have received approval of our New Drug Applications ("NDA") for roxadustat in China for CKD anemia for patients on dialysis and not on dialysis, and for roxadustat in Japan for CKD anemia in dialysis patients, we will need to make substantial additional investments in both the development and commercialization of roxadustat worldwide and in various indications. Our near-term prospects, including maintaining our existing collaborations with Astellas and AstraZeneca, will depend heavily on successful development and commercialization of roxadustat, including obtaining regulatory approvals for the commercialization of roxadustat for anemia associated with CKD in the U.S., Europe, and Japan for non-dialysis patients.

Our other lead product candidate, pamrevlumab, is currently in clinical development for IPF, pancreatic cancer and DMD. Pamrevlumab requires substantial further development and investment. We do not have a collaboration partner for support of this compound, and, while we have promising open-label safety data and potential signals of efficacy, we would need to complete larger and more extensive controlled clinical trials to validate the results to date in order to continue further development of this product candidate. In addition, although there are many potentially promising indications beyond IPF, pancreatic cancer and DMD, we are still exploring indications for which further development of, and investment for, pamrevlumab may be appropriate. Accordingly, the costs and time to complete development and related risks are currently unknown. Moreover, pamrevlumab is a monoclonal antibody, which may require experience and expertise that we may not currently possess as well as financial resources that are potentially greater than those required for our small molecule lead compound, roxadustat.

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, many of which are beyond our control, and we may be unable to complete the development or commercialization of roxadustat or pamrevlumab.*

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, including the following:

- the timely completion of data analyses from our Phase 3 clinical trials for roxadustat, which will depend substantially upon requirements for such trials imposed by the U.S. Food and Drug Administration ("FDA") and other regulatory agencies and bodies and the continued commitment and coordinated and timely performance by our third-party collaboration partners, AstraZeneca and Astellas;
- the timely initiation and completion of our clinical trials for pamrevlumab, including in IPF, pancreatic cancer and DMD;
- our ability to demonstrate the safety and efficacy of our product candidates to the satisfaction of the relevant regulatory authorities;

- the ultimate approval criteria (which may include non-inferiority margins and statistical analyses methods), indications, patient populations, and ultimate benefit-risk analysis used by regulatory authorities in their approval processes;
- whether we are required by the FDA or other regulatory authorities to conduct additional clinical trials, and the scope and nature of such clinical trials, prior to approval to market our products;
- the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities, including pricing and reimbursement determinations:
- the ability to successfully commercialize our product candidates, if approved, for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;
- our ability and the ability of our third-party manufacturing partners to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability;
- our success in educating health care providers and patients about the benefits, risks, administration and use of our product candidates, if approved:
- · acceptance of our product candidates, if approved, as safe and effective by patients and the healthcare community;
- the success of efforts to enter into relationships with large dialysis organizations involving the administration of roxadustat to dialysis
 patients;
- the achievement and maintenance of compliance with all regulatory requirements applicable to our product candidates;
- the maintenance of an acceptable safety profile of our products following any approval;
- the availability, perceived advantages, relative cost, relative safety, and relative efficacy of alternative and competitive treatments;
- our ability to obtain and sustain an adequate level of pricing or reimbursement for our products by third-party payors;
- our ability to enforce successfully our intellectual property rights for our product candidates and against the products of potential competitors; and
- our ability to avoid or succeed in third-party patent interference or patent infringement claims.

Many of these factors are beyond our control. Accordingly, we cannot assure you that we will ever be able to achieve profitability through the sale of, or royalties from, our product candidates. If we or our collaboration partners are not successful in obtaining approval for and commercializing our product candidates, or are delayed in completing those efforts, our business and operations would be adversely affected.

If our commercialization efforts for roxadustat in China are unsuccessful, our business, financial condition and results of operations will be materially harmed.*

We have invested and continue to invest a significant portion of our efforts and financial resources in the development, approval and now commercialization of roxadustat for the treatment of anemia caused by CKD in in China, as well as in other indications and other geographic regions. With the marketing authorization received from the National Medical Products Administration ("NMPA") for roxadustat for the treatment of anemia caused by CKD in patients on dialysis and not on dialysis in China, we plan to launch commercialization efforts in China in the third quarter of 2019 with our commercialization partner AstraZeneca.

Our success of commercialization of roxadustat in China will depend on numerous factors in China, including:

- · our success in the marketing, sales, and distribution of the product along with our collaboration partner AstraZeneca;
- our success in negotiating a cost-effective reimbursed price with the government in China;
- acceptance of roxadustat by state-owned and state-controlled hospitals, physicians, patients and the healthcare community;
- acceptance of pricing and placement of roxadustat on China's Medical Insurance Catalogs. Refer to "Business Government Regulation - Regulation in China" in our annual report on Form 10-K for the year ended December 31, 2018;
- successfully establishing and maintaining commercial manufacturing with third parties;

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- successfully manufacturing our drug substances and drug products through our subsidiary FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing");
- our success in arranging for and passing the inspection of our clinical sites by the NMPA;
- whether AstraZeneca is able to recruit and retain adequate numbers of effective sales and marketing personnel for the sale of roxadustat;
- whether we can compete successfully as a new entrant in the treatment of anemia caused by CKD in dialysis patients and non-dialysis
 patients in China; and
- whether we will maintain sufficient funding to cover the costs and expenses associated with creating and sustaining a capable sales and marketing organization and related commercial infrastructure.

Successful commercialization of roxadustat will require significant resources and time, and there is a risk that we may not successfully commercialize roxadustat. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize roxadustat and generate revenues, which would deprive us from additional working capital and would materially harm our business. If we do not successfully commercialize roxadustat in China, our collaboration partners and third parties may also lose confidence in our ability to execute in commercialization efforts and become less likely to collaborate with us, and our business may be harmed.

As a company, we have no commercialization experience, and the time and resources to develop such experience are significant. If we fail to achieve and sustain commercial success for roxadustat in China, either directly or with AstraZeneca, our business would be harmed.*

Commercializing roxadustat in China with AstraZeneca will require us to establish commercialization systems, including but not limited to, medical affairs, sales, pharmacovigilance, supply-chain, and distribution capabilities to perform our portion of the collaborative efforts. These efforts will require resources and time. In particular, significant resources may be necessary to successfully market, sell and distribute roxadustat to patients with anemia caused by CKD in dialysis patients and non-dialysis patients. If we, along with AstraZeneca, are not successful in setting our marketing, pricing and reimbursement strategy, facilitating adoption by hospitals in China, recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing roxadustat, which would adversely affect our business and financial condition.

As we evolve from a company primarily involved in research and development to a company potentially involved in commercialization, we may encounter difficulties in managing our growth and expanding our operations successfully.

If we are successful in advancing roxadustat and our other product candidates through the development stage towards commercialization, we will need to expand our organization, including adding marketing and sales capabilities or continuing to contract with third parties to provide these capabilities for us. As our operations expand, we expect that we will also need to manage our existing and additional relationships with various collaborative partners, suppliers and other third parties. Future growth will impose significant added responsibilities on our organization, in particular on management. Our future financial performance and our ability to commercialize roxadustat and our other product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we may not be able to manage our growth efforts effectively, and hire, train and integrate additional management, administrative and sales and marketing personnel, and our failure to accomplish any of these activities could prevent us from successfully growing our Company.

Although regulatory approval has been obtained for roxadustat in China and Japan, we may be unable to obtain regulatory approval for our product candidates in other countries, or such approval may be delayed or limited, due to a number of factors, many of which are beyond our control.*

The clinical trials and the manufacturing of our product candidates are and will continue to be, and the marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to develop and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical trials and clinical trials that the product candidate is safe and effective for use in each indication for which approval is sought. The regulatory review and approval process is expensive and requires substantial resources and time, and in general very few product candidates that enter development receive regulatory approval. In addition, our collaboration partners for roxadustat have final control over development decisions in their respective territories and they may make decisions with respect to development or regulatory authorities that delay or limit the potential approval of roxadustat, or increase the cost of development or commercialization. Accordingly, we may be unable to successfully develop or commercialize roxadustat or pamrevlumab or any of our other product candidates.

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Even though regulatory approval has been obtained for roxadustat in China and Japan, we have not obtained regulatory approval for any of our product candidates in other countries and it is possible that roxadustat and pamrevlumab will never receive regulatory approval in other countries. Other regulatory authorities may take actions or impose requirements that delay, limit or deny approval of roxadustat or pamrevlumab for many reasons, including, among others:

- our failure to adequately demonstrate to the satisfaction of regulatory authorities that roxadustat is safe and effective in treating anemia in CKD or that pamrevlumab is safe and effective in treating IPF, pancreatic cancer or DMD;
- our failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the determination by regulatory authorities that additional clinical trials are necessary to demonstrate the safety and efficacy of roxadustat or pamrevlumab, or that ongoing clinical trials need to be modified in design, size, conduct or implementation;
- our product candidates may exhibit an unacceptable safety signal as they advance through clinical trials, in particular controlled Phase 3 trials;
- the clinical research organizations ("CROs") that conduct clinical trials on our behalf may take actions outside of our control that materially adversely impact our clinical trials;
- we or third-party contractors manufacturing our product candidates may not maintain current good manufacturing practices ("cGMP"), successfully pass inspection or meet other applicable manufacturing regulatory requirements;
- · regulatory authorities may not agree with our interpretation of the data from our preclinical trials and clinical trials;
- · collaboration partners may not perform or complete their clinical programs in a timely manner, or at all; or
- principal investigators may determine that one or more serious adverse events ("SAEs"), is related or possibly related to roxadustat,
 and any such determination may adversely affect our ability to obtain regulatory approval, whether or not the determination is correct.

Any of these factors, many of which are beyond our control, could jeopardize our or our collaboration partners' abilities to obtain regulatory approval for and successfully market roxadustat. Because our business and operations in the near-term are almost entirely dependent upon roxadustat, any significant delays or impediments to regulatory approval could have a material adverse effect on our business and prospects.

In China, the NMPA required that FibroGen Beijing conduct three clinical studies as a post-approval commitment: (i) a post-approval safety study in 2,000 patients; (ii) a drug-intensive monitoring study in 1,000 patients; and (iii) a dosing optimization study in approximately 300 patients on dialysis. Furthermore, in the U.S., we also expect to be required to perform additional clinical trials in order to obtain approval or as a condition to maintaining approval due to post-marketing requirements. If the FDA requires a risk evaluation and mitigation strategy ("REMS"), for any of our product candidates if approved, the substantial cost and expense of complying with a REMS or other post-marketing requirements may limit our ability to successfully commercialize our product candidates.

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Preclinical, Phase 1 and Phase 2 clinical trial results may not be indicative of the results that may be obtained in larger, controlled Phase 3 clinical trials required for approval.*

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical and early clinical trials, which are often highly variable and use small sample sizes, may not be predictive of similar results in humans or in larger, controlled clinical trials, and successful results from early or small clinical trials may not be replicated or show as favorable an outcome, even if successful.

We have conducted a limited number of Phase 2 clinical trials with pamrevlumab. We have conducted a randomized placebo-controlled study in 103 IPF patients with sub-studies in an additional 57 IPF patients comparing pamrevlumab to one of two standards of care, an open-label Phase 2 dose escalation study of pamrevlumab for IPF in 89 patients and a randomized double-blind placebo controlled study for liver fibrosis in subjects with hepatitis B, we are currently conducting an open-label randomized, active-control, neoadjuvant Phase 2 trial in pancreatic cancer combining pamrevlumab with nab-paclitaxel plus gemcitabine in 37 patients, and we are currently in a Phase 2 open-label trial of pamrevlumab for DMD in 21 non-ambulatory patients. We cannot be sure that the results we have received to date from these trials will be substantiated in larger, well-controlled Phase 3 clinical trials, that larger trials will demonstrate the safety and efficacy of pamrevlumab for these or other indications, that further studies will provide benefits over existing approved products or that new safety issues will not be uncovered in further trials. In addition, while we believe that the limited animal and human studies conducted to date suggest that pamrevlumab has the potential to arrest or reverse fibrosis and reduce tumor mass in some patients or diseases, we cannot be sure that these results will be indicative of the effects of pamrevlumab in larger human trials. In addition, the IPF and pancreatic cancer patient populations are extremely ill and routinely experience SAEs, including death, which may be attributed to pamrevlumab in a manner that negatively impacts the safety profile of our product candidate. If the additional clinical trials that we are planning or are currently conducting for pamrevlumab do not show favorable efficacy results or result in safety concerns, or if we do not meet our clinical endpoints with statistical significance, or demonstrate an acceptable risk-benefit profile, we may be prevented from or delay

In the past we developed an earlier generation product candidate aimed at treating anemia in CKD that resulted in a clinical hold for a safety signal seen in that product in Phase 2 clinical trials. The clinical hold applied to that product candidate and roxadustat was lifted for both product candidates after submission of the requested information to the FDA. While we have not seen similar safety concerns involving roxadustat to date, some of the safety concerns associated with the treatment of patients with anemia in CKD using erythropoiesis stimulating agents ("ESAs") did not emerge for many years until placebo-controlled studies had been conducted in large numbers of patients. And while the data monitoring committee for our U.S. and Europe Phase 3 anemia trials has consistently determined that our trials should continue without modification to the protocol, safety issues may still be discovered upon review of unblinded major adverse cardiac event ("MACE") or other data. The biochemical pathways that we believe are affected by roxadustat are implicated in a variety of biological processes and disease conditions, and it is possible that the use of roxadustat to treat larger numbers of patients will demonstrate unanticipated adverse effects, including possible drug interactions, which may negatively impact the safety profile, use and market acceptance of roxadustat. We studied the potential interaction between roxadustat and three statins (atorvastatin, rosuvastatin and simvastatin), which are used to lower levels of lipids in the blood. An adverse effect associated with increased statin plasma concentration is myopathy, which typically presents in a form of myalgia. The studies indicated the potential for increased exposure to those statins when roxadustat is taken simultaneously with those statins and suggested the need for statin dose reductions for patients receiving higher statin doses. We performed additional clinical pharmacology studies to evaluate if the effect of any such interaction could be minimized or eliminated by a modification of the dosing schedule that would separate the administration of roxadustat and the statin by up to 10 hours, however, such studies showed no minimization of effect. It is possible that the potential for interaction between roxadustat and statins could lead to label provisions for statins or roxadustat relating, for example, to dose scheduling or recommended statin dose limitations. In CKD patients, statin therapy is often initiated earlier than treatment for anemia, and risks of myopathy have been shown to decrease with increased time on drug. While we believe the prior statin treatment history of such patients at established doses may reduce the risk of adverse effects from any interaction with roxadustat and facilitate any appropriate dose adjustments, we cannot be sure that this will be the case.

Our Phase 3 trials include a MACE safety endpoint, which is a composite endpoint designed to identify major safety concerns, in particular relating to cardiovascular events such as cardiovascular death, myocardial infarction and stroke. The European Medicines Agency ("EMA") is requiring MACE+ as a safety endpoint which, in addition to the MACE components, incorporates measurements of hospitalization rates due to heart failure or unstable angina. The EMA will also review MACE results. The FDA has also informed us that the MACE endpoint will need to be evaluated separately for our Phase 3 trials in non-dialysis-dependent ("NDD")-CKD patients and our Phase 3 trials in dialysis-dependent ("DD")-CKD patients. The MACE endpoint is being evaluated in pooled analysis across Phase 3 studies of similar study populations and requires demonstration of non-inferiority relative to comparator, which means that the MACE event rate in roxadustat-treated patients must have less than a specified probability of exceeding the rate in the comparator trial by a specified hazard ratio.

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The number of patients necessary in order to permit a statistical analysis with adequate ability to detect the relative risk of MACE or MACE+ events in different arms of the trial, referred to as statistical power, depends on a number of factors, including the rate at which MACE or MACE+ events occur per patient-year in the trial, treatment duration of the patients, the achieved hazard ratios, the rates of discontinuation, and the required statistical power and confidence intervals.

In addition, we cannot be sure that the potential advantages we believe roxadustat may have for treatment of patients with anemia in CKD, as compared to the use of ESAs, will be substantiated by our larger U.S. and European Phase 3 clinical trials, or that we will be able to include a discussion of such advantages in our labeling should we obtain approval. We believe that roxadustat may have certain benefits as compared to ESAs based on the data from our Phase 2 clinical trials and China Phase 3 trials conducted to date, including safety benefits, the absence of a hypertensive effect, the potential to lower cholesterol levels and the potential to correct anemia without the use of IV iron. However, our belief that roxadustat may offer those benefits is based on a limited amount of data from our clinical trials to date, and our understanding of the likely mechanisms of action for roxadustat. Some of these benefits, such as those associated with the apparent effects on blood pressure and cholesterol, are not fully understood and, even if roxadustat receives marketing approval in additional countries beyond China and Japan, we do not expect that it will be approved for the treatment of high blood pressure or high cholesterol based on the data from our Phase 3 trials, and we may not be able to refer to any such benefits in the labeling. While the data from our Phase 2 trials suggests roxadustat may reduce low-density lipoprotein ("LDL"), and reduce the ratio of LDL to high-density lipoprotein ("HDL"), the data show it may also reduce HDL, which may be a risk to patients. In addition, causes of the safety concerns associated with the use of ESAs to achieve specified target hemoglobin levels have not been fully elucidated. While we believe that the issues giving rise to these concerns with ESAs are likely due to factors other than the hemoglobin levels achieved, we cannot be certain that roxadustat will not be associated with similar, or more severe, safety concerns.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may face similar setbacks. In addition, the CKD patient population has many afflictions that may cause severe illness or death, which may be attributed to roxadustat in a manner that negatively impacts the safety profile of our product candidate. The results of our completed Phase 3 clinical trials for roxadustat demonstrated efficacy, as all primary efficacy endpoints were met with statistical significance. While we have reported topline cardiovascular safety results, the analysis of these data is ongoing; there may be unanticipated safety concerns or adverse events that prevent from or delay obtaining marketing approval for roxadustat in additional countries beyond China and Japan, and even if we obtain marketing approval, any sales of roxadustat may suffer.

We do not know whether our ongoing or planned clinical trials of roxadustat or pamrevlumab will need to be redesigned based on interim results, be able to achieve sufficient enrollment or be completed on schedule, if at all.*

Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- address any physician or patient safety concerns that arise during the course of the trial;
- obtain required regulatory or institutional review board ("IRB") approval or guidance;
- reach timely agreement on acceptable terms with prospective CROs and clinical trial sites;
- recruit, enroll and retain patients through the completion of the trial;
- maintain clinical sites in compliance with clinical trial protocols;
- initiate or add a sufficient number of clinical trial sites; and
- manufacture sufficient quantities of product candidate for use in clinical trials.

In addition, we could encounter delays if a clinical trial is suspended or terminated by us, by the relevant IRBs at the sites at which such trials are being conducted, or by the FDA or other regulatory authorities. A suspension or termination of clinical trials may result from any number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or a principal investigator's determination that a serious adverse event could be related to our product candidates. Any delays in completing our clinical trials will increase the costs of the trial, delay the product candidate development and approval process and jeopardize our ability to commence marketing and generate revenues. Any of these occurrences may materially and adversely harm our business and operations and prospects.

Our product candidates may cause or have attributed to them undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our product candidates or that may be identified as related to our product candidates by physician investigators conducting our clinical trials or even competing products in development that utilize a similar mechanism of action or act through a similar biological disease pathway could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. Adverse events and SAEs that emerge during treatment with our product candidates or other compounds acting through similar biological pathways may be deemed to be related to our product candidate and may result in:

- our Phase 3 clinical trial development plan becoming longer and more extensive;
- regulatory authorities increasing the data and information required to approve our product candidates and imposing other requirements; and
- our collaboration partners terminating our existing agreements.

The occurrence of any or all of these events may cause the development of our product candidates to be delayed or terminated, which could materially and adversely affect our business and prospects. Refer to "Business - Our Development Program for Roxadustat" and "Business - Pamrevlumab for the Treatment of Fibrosis and Cancer" for a discussion of the adverse events and SAEs that have emerged in clinical trials of roxadustat and pamrevlumab.

Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.

Clinical trials are conducted in representative samples of the potential patient population, which may have significant variability. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, that a more complete safety profile is identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. There have been other products, including ESAs, for which safety concerns have been uncovered following approval by regulatory authorities. Such safety concerns have led to labeling changes or withdrawal of ESAs products from the market. While our most advanced product candidate is chemically unique from ESAs, it or any of our product candidates may be subject to similar risks. For example, roxadustat for use in anemia in CKD is being developed to address a very diverse patient population expected to have many serious health conditions at the time of administration of roxadustat, including diabetes, high blood pressure and declining kidney function.

To date we have not seen evidence of significant safety concerns with our product candidates currently in clinical trials. Patients treated with our products, if approved, may experience adverse reactions and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If safety problems occur or are identified after our product candidates reach the market, we may, or regulatory authorities may require us to amend the labeling of our products, recall our products or even withdraw approval for our products.

We may fail to enroll a sufficient number of patients in our clinical trials in a timely manner, which could delay or prevent clinical trials of our product candidates.

Identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the rate at which we can recruit and enroll patients in testing our product candidates. Patients may be unwilling to participate in clinical trials of our product candidates for a variety of reasons, some of which may be beyond our control:

- severity of the disease under investigation;
- availability of alternative treatments;
- size and nature of the patient population;
- eligibility criteria for and design of the study in question;
- perceived risks and benefits of the product candidate under study;
- ongoing clinical trials of competitive agents;

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- physicians' and patients' perceptions of the potential advantages of our product candidates being studied in relation to available therapies or other products under development;
- our CRO's and our trial sites' efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients and collect patient data adequately during and after treatment.

Patients may be unwilling to participate in our clinical trials for roxadustat due to adverse events observed in other drug treatments of anemia, and patients currently controlling their disease with existing ESAs may be reluctant to participate in a clinical trial with an investigational drug. We may not be able to successfully initiate or continue clinical trials if we cannot rapidly enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate on-going or planned clinical trials, any of which could have a material and adverse effect on our business and prospects.

If we or third-party manufacturers and other service providers on which we rely cannot manufacture sufficient quantities of our product candidates, or at sufficient quality, or perform other services we require, we may experience delays in development, regulatory approval, launch or commercialization.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture and manage our product candidates at sufficient yields and at commercial scale. Although we have entered into commercial supply agreements for the manufacture of some of our raw materials, we have not yet entered into commercial supply agreements with all of our third-party manufacturers. We are continuing to negotiate and expect to enter into commercial supply agreements and other supply management agreements with third-party manufacturers, but we may not be able to enter into these agreements with satisfactory terms or on a timely manner.

We have limited experience manufacturing or managing third parties in manufacturing any of our product candidates in the volumes that are expected to be necessary to support large-scale clinical trials and sales. In addition, we have limited experience forecasting supply requirements or coordinating supply chain (including export management) for launch or commercialization, which is a complex process involving our third-party manufacturers and logistics providers, and for roxadustat, our collaboration partners. We may not be able to accurately forecast supplies for commercial launch, or do so in a timely manner and our efforts to establish these manufacturing and supply chain management capabilities may not meet our requirements as to quantities, scale-up, yield, cost, potency or quality in compliance with cGMP.

We have a limited amount of roxadustat and pamrevlumab in storage, limited capacity reserved at our third-party manufactures, and there are long lead times required to manufacture and scale-up the manufacture of additional supply, as required for both late-stage clinical trials, post-approval trials, and commercial supply. If we are unable to forecast, order or manufacture sufficient quantities of roxadustat or pamrevlumab on a timely basis, it may delay our development, launch or commercialization in some or all indications we are currently pursuing. For example, prior to agreement with regulatory authorities on the scope of our Phase 3 IPF trial design, there is uncertainty as to whether our supply plans will meet our clinical requirements in a timely manner. Any delay or interruption in the supply of our product candidates or products could have a material adverse effect on our business and operations.

Our clinical trials must be conducted with product produced under applicable cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We, and even an experienced third-party manufacturer, may encounter difficulties in production. Difficulties may include:

- costs and challenges associated with scale-up and attaining sufficient manufacturing yields, in particular for biologic products such as pamrevlumab, which is a monoclonal antibody;
- supply chain issues, including coordination of multiple contractors in our supply chain and securing necessary licenses (such as export licenses);
- the timely availability and shelf life requirements of raw materials and supplies;
- · quality control and quality assurance;
- shortages of qualified personnel and capital required to manufacture large quantities of product;

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- · compliance with regulatory requirements that vary in each country where a product might be sold;
- · capacity or forecasting limitations and scheduling availability in contracted facilities; and
- natural disasters, such as floods, storms, earthquakes, tsunamis, and droughts, or accidents such as fire, that affect facilities, possibly limit or postpone production, and increase costs.

The FDA and EMA will do their own benefit risk analysis and may reach a different conclusion than we or our partners have internally, and these regulatory authorities may base their approval decision on different analyses, data, and statistical methods than ours.*

Even if we believe we have achieved certain results based on a totality of the evidence, such as superiority or non-inferiority, in certain endpoints, populations or subpopulations, or using certain statistical methods of analysis, the FDA and EMA will each conduct their own benefit-risk analysis and may reach different conclusions, using different statistical methods, different endpoints or definitions thereof, or different patient populations or sub-populations, and regulatory authorities may change their approvability criteria based on their internal analyses and discussions with expert advisors. Regulatory authorities may approve roxadustat for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-approval clinical trials. While we will present to regulatory authorities certain pre-specified and not pre-specified sub-populations and sub-group analyses (for example, incident dialysis), multiple secondary endpoints, and multiple analytical methods (such as long-term follow up analyses), including adjusted and censored data, regulatory authorities may reject these analyses, methods, or even parts of our trial design or certain data from our studies, the rationale for our pre-specified non-inferiority margins or other portions of our statistical analysis plans. In addition, even if we are able to provide positive data with respect to certain analyses, such as incident dialysis, estimated glomerular filtration rate, hepcidin, or quality of life measures, regulatory authorities may not include such claims on any approved labeling for roxadustat, which may limit the commercialization or market opportunity for roxadustat. Further, initial topline results reported for certain studies (such as reduction of transfusion risk or hemoglobin response in the presence of inflammation), may not be representative of the data seen in all studies or may not be sustained upon further analyses or after more wide-spread use upon commercialization. The failure to obtain regulatory approval, or any label, population or other approval limitations in any jurisdiction, may significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenue.

Positive topline results from our Phase 3 clinical trials assessing the safety and efficacy of roxadustat may not be indicative of additional results or results for roxadustat in other indications.*

There are multiple key and secondary endpoints as well as sub-group analyses in both dialysis and non-dialysis in the U.S. and multiple secondary endpoints in addition to MACE+ as well as sub-group analyses in dialysis and non-dialysis in Europe. We continue to analyze these additional endpoints from the Phase 3 clinical trials of roxadustat in anemia of CKD, as well as from the pooled analyses, some of which may have a bearing on the safety or efficacy of roxadustat. The topline results we have reported thus far may not be indicative of these additional results. In addition, results in these CKD-anemia indications may not be indicative of our clinical trials in other indications or the safety, efficacy, or approvability of roxadustat in other indications. If these topline results are not indicative of additional results or results in other indications, our potential revenue may be reduced.

Even if we are able to obtain regulatory approval of our product candidates, the label we obtain may limit the indicated uses for which our product candidates may be marketed.*

With respect to roxadustat, regulatory approvals obtained outside of China and Japan, could limit the approved indicated uses for which roxadustat may be marketed. For example, ESAs have been subject to significant safety warnings, including the "Black Box" warnings on their labels. Refer to "Business - Roxadustat for the Treatment of Anemia in Chronic Kidney Disease - Limitations of the Current Standard of Care for Anemia in CKD" in our annual report on Form 10-K for the year ended December 31, 2018. In addition, in the past, an approved ESA was voluntarily withdrawn due to serious safety issues discovered after approval. The safety concerns relating to ESAs may result in labeling for roxadustat containing similar warnings even if our Phase 3 clinical trials do not suggest that roxadustat has similar safety issues. Even if the label for roxadustat does not contain all of the warnings contained in the "Black Box" warning for ESAs, the label for roxadustat may contain other warnings or limit the market opportunity or approved indications for roxadustat. These warnings could include warnings against exceeding specified hemoglobin targets and other warnings that derive from the lack of clarity regarding the safety issues associated with ESAs, even if our Phase 3 clinical trials do not themselves raise safety concerns.

As an organization, we have not successfully commercialized any drug product. Therefore, we may not be able to efficiently execute our development and commercialization plans.*

We are currently conducting Phase 3 clinical trials for pamrevlumab and roxadustat. The conduct of Phase 3 clinical trials and the submission of a successful NDA is a complicated process. As an organization, we have limited experience in preparing, submitting and prosecuting regulatory filings, and have not received approval for an NDA outside of China, where we received marketing authorization from the NMPA for the treatment of anemia caused by CKD in dialysis patients and non-dialysis patients, and Japan, where the Ministry of Health, Labour and Welfare approved roxadustat for the treatment of CKD in dialysis patients. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials and regulatory submissions in other countries or for any other product candidate we are developing, even if our earlier stage clinical trials are successful. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials would prevent us from or delay us in commercializing product candidates we are developing.

In addition, in order for any Phase 3 clinical trial to support an NDA submission for approval, the FDA and foreign regulatory authorities require compliance with regulations and standards, including good clinical practices ("GCP") requirements for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials to ensure that the data and results from trials are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we as the sponsor remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or other regulatory authorities may require us to exclude the use of patient data from our clinical trials not conducted in compliance with GCP or perform additional clinical trials before approving our marketing applications. They may even reject our application for approval or refuse to accept our future applications for an extended time period. For example in China in March 2016, the State Drug Administration, now known as the NMPA issued guidance related to its clinical trial data integrity regulations. While trial sites and CROs bear liability for the accuracy and authenticity of data they are directly responsible for, the sponsor ultimately bears full responsibility for submitted clinical data and the drug application dossier. Fraudulent clinical data could result in a ban in China of a sponsor's product-related NDA applications for three years and other NDA applications for one year. We have taken extensive steps to ensure the integrity of our China clinical data. In China, the clinical site inspections confirmed our compliance with GCP regulations and supported our approval. However, we cannot assure you that upon inspection by a regulatory authority in other regions, such regulatory authority will determine that any of our clinical trials comply with GCP requirements or that our results will be deemed authentic or may be used in support of our regulatory submissions.

If we are unable to establish sales, marketing and distribution capabilities or enter into or maintain agreements with third parties to market and sell our product candidates, we may not be successful in commercializing our product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sales, marketing or distribution of pharmaceutical products in any country. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales and marketing capabilities or make and maintain our existing arrangements with third parties to perform these services at a level sufficient to support our commercialization efforts.

To the extent that we would undertake sales and marketing of any of our products directly, there are risks involved with establishing our own sales, marketing and distribution capabilities. Factors that may inhibit our efforts to commercialize our products on our own include:

- · our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products:
- our inability to effectively manage geographically dispersed sales and marketing teams;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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With respect to roxadustat, we are dependent on the commercialization capabilities of our collaboration partners, AstraZeneca and Astellas. If either such partner were to terminate its agreement with us, we would have to commercialize on our own or with another third party. We will have limited or little control over the commercialization efforts of such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products, if any, effectively. If they are not successful in commercializing our product candidates, our business and financial condition would suffer.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.*

The development and commercialization of new pharmaceutical products is highly competitive. Our future success depends on our ability to achieve and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to discover, develop and commercialize new products with superior efficacy, convenience, tolerability, and safety. We expect that in many cases, the products that we commercialize will compete with existing, market-leading products of companies that have large, established commercial organizations.

If roxadustat is approved and launched commercially, competing drugs are expected to include ESAs, particularly in those patient segments where ESAs are used. Currently available ESAs include epoetin alfa (EPOGEN ®, marketed by Amgen Inc. in the U.S., Procrit ® and Erypo ®/Eprex ®, marketed by Johnson & Johnson Inc., and Espo ® marketed by Kyowa Hakko Kirin in Japan and China), darbepoetin (Amgen/Kyowa Hakko Kirin's Aranesp ® and NESP ®) and Mircera ® marketed by Hoffmann-La Roche ("Roche") outside of the U.S. and by Vifor Pharma ("Vifor"), a Roche licensee, in the U.S. and Puerto Rico, as well as biosimilar versions of these currently marketed ESA products. ESAs have been used in the treatment of anemia in CKD for more than 20 years, serving a significant majority of DD-CKD patients. While NDD-CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated, some patients under nephrology care may be receiving ESA therapy. It may be difficult to encourage healthcare providers and patients to switch to roxadustat from products with which they have become familiar.

We may also face competition from potential new anemia therapies currently in clinical development, including in those patient segments not currently addressed by ESAs. Companies such as GlaxoSmithKline plc ("GSK"), Bayer Corporation ("Bayer"), Akebia Therapeutics, Inc. ("Akebia"), and Japan Tobacco Inc., are currently developing HIF prolyl hydroxylase ("HIF-PH") inhibitors for anemia in CKD indications. Akebia has completed enrollment in its global Phase 3 studies in NDD-CKD and DD-CKD, while conducting additional Phase 1 and Phase 2 studies. In Japan, Mitsubishi Tanabe Pharmaceutical Corporation ("Mitsubishi Tanabe"), Akebia's collaboration partner, submitted an NDA in July 2019 for treatment of anemia in CKD patients on dialysis and not on dialysis, supported by the Phase 3 studies conducted by Mitsubishi Tanabe in Japan. GSK is conducting global Phase 3 studies in NDD-CKD and DD-CKD. In Japan, GSK submitted an NDA in August 2019 for the treatment of patients with renal anemia due to CKD. GSK and Kyowa Hakko Kirin announced in November 2018 that the two companies signed a strategic commercialization deal in Japan for daprodustat. Bayer has completed global Phase 2 studies and announced in May 2017 its HIF-PH inhibitor is now in continued development in Japan only, and its Japan Phase 3 studies in NDD-CKD and DD-CKD are expected to complete in the second half of 2019. Japan Tobacco Inc. is also conducting Phase 3 studies in NDD-CKD and DD-CKD in Japan only. Some of these product candidates may enter the market prior to roxadustat.

In addition, there are other companies developing biologic therapies for the treatment of other anemia indications that we may also seek to pursue in the future, including anemia of MDS. For example, Acceleron Pharma Inc. and its partner Celgene Corporation ("Celgene") announced in June 2019 that the U.S. FDA accepted Celgene's Biologics License Application ("BLA") for luspatercept for the treatment of adult patients with very low to intermediate risk of MDS-associated anemia who have ring sideroblasts and require red blood cell transfusions for regular review, and beta-thalassemia-associated anemia who require red blood cell transfusions for priority review, with the target action dates of April 2020 and December 2019, respectively. Celgene's marketing approval application for luspatercept has also been accepted by the European Union ("EU"), and a luspatercept Phase 2 study started in Japan. There may also be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat if and when it is commercialized.

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In China, locally manufactured epoetin alfa are offered by Chinese pharmaceutical companies such as EPIAO marketed by 3SBio Inc. as well as more than 15 other local manufacturers. We may also face competition by HIF-PH inhibitors from other companies such as Akebia, Bayer, and GSK, which was authorized by the NMPA to conduct trials in China to support its ex-China regulatory filings. Furthermore, while it is too early to understand how the NMPA will implement its recently approved guidelines to allow multinational companies to use their ex-China clinical data in their NDAs in China, these guidelines could in theory allow competitors to accelerate their NDA applications in China. Akebia announced in December 2015 that it has entered into a development and commercialization partnership with Mitsubishi Tanabe for its HIF-PH inhibitor vadadustat in Japan, Taiwan, South Korea, India, and certain other countries in Asia, and announced in April 2017 an expansion of their U.S. collaboration with Otsuka to add markets, including China. Two Chinese domestic companies, Jiangsu Hengrui Medicine Co., Ltd. and Guangdong Sunshine Health Investment Co., Ltd., have announced they also secured the NMPA approval to conduct clinical trials for their respective HIF-PH inhibitors. 3SBio Inc. has recently filed an IND for its HIF-PH inhibitor with the NMPA.

The first biosimilar ESAs, Pfizer's Retacrit® (epoetin zeta), entered the U.S. market in November 2018. Market penetration of Retacrit® (epoetin zeta) and the potential addition of other biosimilar ESAs, currently under development, may alter the competitive and pricing landscape of anemia therapy in DD-CKD patients under the end stage renal disease bundle. The patents for Amgen's epoetin alfa, EPOGEN, expired in 2004 in the EU, and the final material patents in the U.S. expired in May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in the EU, China and other territories. In the U.S., a few ESA biosimilars are currently under development. Sandoz, a division of Novartis, markets Binocrit® (epoetin alfa) in Europe and may file a biosimilar BLA in the U.S.

The majority of the current CKD anemia market focuses on dialysis patients, who visit dialysis centers on a regular basis, typically three-times a week, and anemia therapies are administered as part of the visit. Two of the largest operators of dialysis clinics in the U.S., DaVita Healthcare Partners Inc. ("DaVita") and Fresenius Medical Care AG & Co. KGaA ("Fresenius"), collectively provide dialysis care to over 80% of U.S. dialysis patients, and therefore have historically won long-term contracts including rebate terms with Amgen. In January 2017, DaVita entered into a new 6-year sourcing and supply agreement with Amgen that is effective through 2022. Fresenius' contract with Amgen expired in 2015, and Fresenius is now administering Mircera® in a significant portion of its U.S. dialysis patients since Mircera was made available by Vifor. Successful penetration of this market may require a significant agreement with Fresenius or DaVita on favorable terms and on a timely basis.

If pamrevlumab is approved and launched commercially to treat IPF, competing drugs are expected to include Roche's Esbriet® (pirfenidone) and Boehringer Ingelheim Pharma GmbH & Co. KG's Ofev® (nintedanib). Nintedanib is also in development for non-small cell lung cancer and ovarian cancer. Other potential competitive product candidates in development for IPF include Biogen-Idec's BG-00011, Galapagos NV's GLPG1690 and GLPG1205, Kadmon Holdings, Inc.'s KD025, Prometic Life Sciences Inc.'s PBI-4050, and Promedior Inc.'s PRM-151. Galapagos NV initiated a Phase 3 study for GLPG 1690 in December 2018.

If pamrevlumab is approved and launched commercially to treat locally advanced pancreatic cancer patients who are not candidates for surgical resection, pamrevlumab may face competition from agents seeking approval in combination with gemcitibine and nab-paclitaxel from companies such as NewLink Genetics Corporation and Halozyme Therapeutics, Inc. Gemcitabine and/or nab-paclitaxel are the current standard of care in the first-line treatment of metastatic pancreatic cancer. Celgene Corporation's Abraxane® (nab-paclitaxel) was launched in the U.S. and Europe in 2013 and 2014, and was the first drug approved in this disease in nearly a decade.

If pamrevlumab is approved and launched commercially to treat DMD, pamrevlumab may face competition for some patients from Sarepta Therapeutics, Inc. ("Sarepta") with Exondys 51® (eteplirsen), approved in the U.S. for patients who have a confirmed mutation in the DMD gene that is amenable to exon 51 skipping, and from PTC Therapeutics' drug ataluren approved in ambulatory patients in Europe. We may also face competition from Sarepta's golodirsen, currently under NDA review in the U.S., and agents currently in development for DMD, including PTC Therapeutics, Inc.'s ataluren, Santhera Pharmaceuticals Holding's idebone, Catabasis Pharmaceuticals, Inc.'s edasalonexent, Capricor Therapeutics Inc.'s CAP-1002, and Sarepta's casimersen and other gene therapies, if and when these agents are approved and launched.

The success of any or all of these potential competitive products may negatively impact the development and potential for success of pamrevlumab. In addition, any competitive products that are on the market or in development may compete with pamrevlumab for patient recruitment and enrollment for clinical trials or may force us to change our clinical trial design, including, in order to compare pamrevlumab against another drug, which may be the new standard of care.

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If FG-5200 is approved and launched in China to treat corneal blindness resulting from partial thickness corneal damage without active inflammation and infection, it is likely to compete with other products designed to treat corneal damage. For example, in April 2015, a subsidiary of China Regenerative Medicine International Limited received approval for their acellular porcine cornea stroma medical device to treat patients in China with corneal ulcers and in April 2016, Guangzhou Yourvision Biotech Co. Ltd, a subsidiary of Guanhao Biotech, received approval for their acellular porcine cornea medical device to treat patients in China with infectious keratitis that does not respond to drug treatment.

Moreover, many of our competitors have significantly greater resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients, manufacturing pharmaceutical products, and commercialization. In the potential anemia market for roxadustat, for example, large and established companies such as Amgen and Roche, among others, compete aggressively to maintain their market shares. In particular, the currently marketed ESA products are supported by large pharmaceutical companies that have greater experience and expertise in commercialization in the anemia market, including in securing reimbursement, government contracts and relationships with key opinion leaders; conducting testing and clinical trials; obtaining and maintaining regulatory approvals and distribution relationships to market products; and marketing approved products. These companies also have significantly greater scale, research and marketing capabilities than we do and may also have products that have been approved or are in later stages of development and have collaboration agreements in our target markets with leading dialysis companies and research institutions. These competitors have in the past successfully prevented new and competing products from entering the anemia market, and we expect that their resources will represent challenges for us and our collaboration partners, AstraZeneca and Astellas. If we and our collaboration partners are not able to compete effectively against existing and potential competitors, our business and financial condition may be materially and adversely affected.

Our future commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, third-party payors and others in the health care community.

Even if we obtain marketing approval for roxadustat, pamrevlumab or any other product candidates that we may develop or acquire in the future in all indications and geographic regions, these product candidates may not gain market acceptance among physicians, third-party payors, patients and others in the health care community. Market acceptance of any approved product, including in roxadustat for the treatment of anemia caused by CKD in China and Japan, depends on a number of other factors, including:

- the clinical indications for which the product is approved and the labeling required by regulatory authorities for use with the product, including any warnings that may be required in the labeling;
- acceptance by physicians and patients of the product as a safe and effective treatment and the willingness of the target patient population to try new therapies and of physicians to prescribe new therapies;
- the cost, safety, efficacy and convenience of treatment in relation to alternative treatments;
- the restrictions on the use of our products together with other medications, if any;
- the availability of adequate coverage and reimbursement or pricing by third-party payors and government authorities;
- the ability of treatment providers, such as dialysis clinics, to enter into relationships with us without violating their existing agreement;
- the effectiveness of our sales and marketing efforts.

No or limited reimbursement or insurance coverage of our approved products, if any, by third-party payors may render our products less attractive to patients and healthcare providers.

Market acceptance and sales of any approved products will depend significantly on reimbursement or coverage of our products by the Chinese government or third-party payors and may be affected by existing and future healthcare reform measures or prices of related products for which the government or third-party reimbursement applies. Coverage and reimbursement by the government or a third-party payor may depend upon a number of factors, including the payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

The review and publication cycle for the Chinese government to update their reimbursement lists (national or provincial) is unpredictable and is outside our control.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor, which we may not be able to provide. Furthermore, the reimbursement policies of third-party payors may significantly change in a manner that renders our clinical data insufficient for adequate reimbursement or otherwise limits the successful marketing of our products. Even if we obtain coverage for our product candidates, third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. If reimbursement is not available or is available only to limited levels, we may not be able to commercialize certain of our products.

Price controls may limit the price at which products such as roxadustat, if approved, are sold. For example, reference pricing is used by various EU member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partner may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unacceptable levels, we or our partner may elect not to commercialize our products in such countries, and our business and financial condition could be adversely affected.

Risks Related to Our Reliance on Third Parties

If our collaborations with Astellas or AstraZeneca were terminated, or if Astellas or AstraZeneca were to prioritize other initiatives over their collaborations with us, whether as a result of a change of control or otherwise, our ability to successfully develop and commercialize our lead product candidate, roxadustat, would suffer.

We have entered into collaboration agreements with respect to the development and commercialization of our lead product candidate, roxadustat, with Astellas and AstraZeneca. These agreements provide for reimbursement of our development costs by our collaboration partners and also provide for commercialization of roxadustat throughout the major territories of the world.

Our agreements with Astellas and AstraZeneca provide each of them with the right to terminate their respective agreements with us, upon the occurrence of negative clinical results, delays in the development and commercialization of our product candidates or adverse regulatory requirements or guidance. The termination of any of our collaboration agreements would require us to fund and perform the further development and commercialization of roxadustat in the affected territory, or pursue another collaboration, which we may be unable to do, either of which could have an adverse effect on our business and operations. In addition, each of those agreements provides our respective partners the right to terminate any of those agreements upon written notice for convenience. Moreover, if Astellas or AstraZeneca, or any successor entity, were to determine that their collaborations with us are no longer a strategic priority, or if either of them or a successor were to reduce their level of commitment to their collaborations with us, our ability to develop and commercialize roxadustat could suffer. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaboration agreements with other parties in the area or field of exclusivity.

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If we fail to establish and maintain strategic collaborations related to our product candidates, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise at significant cost. This in turn may negatively affect the development of our other product candidates as we direct resources to our most advanced product candidates.

Conflicts with our collaboration partners could jeopardize our collaboration agreements and our ability to commercialize product candidates.

Our collaboration partners have certain rights to control decisions regarding the development and commercialization of our product candidates with respect to which they are providing funding. If we have a disagreement over strategy and activities, our plans for obtaining approval may be revised and negatively affect the anticipated timing and potential for success of our product candidates. Even if a product under a collaboration agreement is approved, we will remain substantially dependent on the commercialization strategy and efforts of our collaboration partners, and neither of our collaboration partners has experience in commercialization of a novel drug such as roxadustat in the dialysis market.

With respect to our collaboration agreements for roxadustat, there are additional complexities in that we and our collaboration partners, Astellas and AstraZeneca, must reach consensus on our Phase 3 development program. Multi-party decision-making is complex and involves significant time and effort, and there can be no assurance that the parties will cooperate or reach consensus, or that one or both of our partners will not ask to proceed independently in some or all of their respective territories or functional areas of responsibility in which the applicable collaboration partner would otherwise be obligated to cooperate with us. Any disputes or lack of cooperation with us by either Astellas or AstraZeneca may negatively impact the timing or success of our planned Phase 3 clinical studies.

We intend to conduct proprietary research programs in specific disease areas that are not covered by our collaboration agreements. Our pursuit of such opportunities could, however, result in conflicts with our collaboration partners in the event that any of our collaboration partners takes the position that our internal activities overlap with those areas that are exclusive to our collaboration agreements, and we should be precluded from such internal activities. Moreover, disagreements with our collaboration partners could develop over rights to our intellectual property. In addition, our collaboration agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaboration partners could lead to the termination of our collaboration agreements, delay collaborative activities, reduce our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaboration partners.

Certain of our collaboration partners could also become our competitors in the future. If our collaboration partners develop competing products, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our product candidates, the development and commercialization of our product candidates and products could be delayed.

We rely on third parties for the conduct of most of our preclinical and clinical trials for our product candidates, and if our third-party contractors do not properly and successfully perform their obligations under our agreements with them, we may not be able to obtain or may be delayed in receiving regulatory approvals for our product candidates.

We rely heavily on university, hospital, dialysis centers and other institutions and third parties, including the principal investigators and their staff, to carry out our clinical trials in accordance with our clinical protocols and designs. We also rely on a number of third-party CROs to assist in undertaking, managing, monitoring and executing our ongoing clinical trials, including those for roxadustat. We expect to continue to rely on CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our development efforts in the future, including our Phase 3 development program for roxadustat. We compete with many other companies for the resources of these third parties, and large pharmaceutical companies often have significantly more extensive agreements and relationships with such third-party providers, and such third-party providers may prioritize the requirements of such large pharmaceutical companies over ours. The third parties on whom we rely may terminate their engagements with us at any time, which may cause delay in the development and commercialization of our product candidates. If any such third party terminates its engagement with us or fails to perform as agreed, we may be required to enter into alternative arrangements, which would result in significant cost and delay to our product development program. Moreover, our agreements with such third parties generally do not provide assurances regarding employee turnover and availability, which may cause interruptions in the research on our product candidates by such third parties.

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Moreover, while our reliance on these third parties for certain development and management activities will reduce our control over these activities, it will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP requirements for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results from trials are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we, as the sponsor, remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites.

If any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, other regulations, trial protocol or other requirements under their agreements with us, the quality or accuracy of the data they obtain may be compromised or unreliable, and the trials of our product candidates may not meet regulatory requirements. If trials do not meet regulatory requirements or if these third parties need to be replaced, the development of our product candidates may be delayed, suspended or terminated, regulatory authorities may require us to exclude the use of patient data from our approval applications or perform additional clinical trials before approving our marketing applications. Regulatory authorities may even reject our application for approval or refuse to accept our future applications for an extended time period. We cannot assure that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements or that our results may be used in support of our regulatory submissions. If any of these events occur, we may not be able to obtain regulatory approval for our product candidates on a timely basis, at a reasonable cost, or at all.

We currently rely, and expect to continue to rely, on third parties to conduct many aspects of our clinical studies and product manufacturing, and these third parties may not perform satisfactorily.

We do not have operating manufacturing facilities at this time other than our roxadustat and FG-5200 manufacturing facility in China, and our current commercial manufacturing facility plans in China are not expected to satisfy the requirements necessary to support development and commercialization outside of China. Other than in and for China specifically, we do not expect to independently manufacture our products. We currently rely, and expect to continue to rely, on third parties to scale-up, manufacture and supply roxadustat and our other product candidates outside of China. Risks arising from our reliance on third-party manufacturers include:

- reduced control and additional burdens of oversight as a result of using third-party manufacturers for all aspects of manufacturing activities, including regulatory compliance and quality control and quality assurance;
- termination of manufacturing agreements, termination fees associated with such termination, or nonrenewal of manufacturing
 agreements with third parties may negatively impact our planned development and commercialization activities;
- · the possible misappropriation of our proprietary technology, including our trade secrets and know-how; and
- disruptions to the operations of our third-party manufacturers or suppliers unrelated to our product, including the merger, acquisition, or bankruptcy of a manufacturer or supplier or a catastrophic event affecting our manufacturers or suppliers.

Any of these events could lead to development delays or failure to obtain regulatory approval or affect our ability to successfully commercialize our product candidates. Some of these events could be the basis for action by the FDA or another regulatory authority, including injunction, recall, seizure or total or partial suspension of production.

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The facilities used by our contract manufacturers to manufacture our product candidates must pass inspections by the FDA and other regulatory authorities. Although, except for China, we do not control the manufacturing operations of, and expect to remain completely dependent on, our contract manufacturers for manufacture of drug substance and finished drug product, we are ultimately responsible for ensuring that our product candidates are manufactured in compliance with cGMP requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our or our collaboration partners' specifications, or the regulatory requirements of the FDA or other regulatory authorities, we may not be able to secure and/or maintain regulatory approval for our product candidates and our development or commercialization plans may be delayed. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. In addition, although our longer-term agreements are expected to provide for requirements to meet our quantity and quality requirements to manufacture our products candidates for clinical studies and commercial sale, we will have minimal direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel and we expect to rely on our audit rights to ensure that those qualifications are maintained to meet our requirements. If our contract manufacturers' facilities do not pass inspection by regulatory authorities, or if regulatory authorities do not approve these facilities for the manufacture of our products, or withdraw any such approval in the future, we would need to identify and qualify alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products, if approved. Moreover, any failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or adverse regulatory consequences, including clinical holds, warnings or untitled letters, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which would be expected to significantly and adversely affect supplies of our products to us and our collaboration partners.

Any of our third-party manufacturers may terminate their engagement with us at any time and we have not yet entered into any commercial supply agreements for the manufacture of active pharmaceutical ingredient ("API") or drug products. With respect to roxadustat, AstraZeneca and Astellas have certain rights to assume manufacturing of roxadustat and the existence of those rights may limit our ability to enter into favorable long-term supply agreements, if at all, with other third-party manufacturers. In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access and prioritization to manufacture. Certain third-party manufacturers may be contractually prohibited from manufacturing our product due to non-compete agreements with our competitors or a commitment to grant another party priority relative to our products. There are a limited number of third-party manufacturers that operate under cGMP and that might be capable of manufacturing to meet our requirements. Due to the limited number of third-party manufacturers with the contractual freedom, expertise, required regulatory approvals and facilities to manufacture our products on a commercial scale, identifying and qualifying a replacement third-party manufacturer would be expensive and time-consuming and may cause delay or interruptions in the production of our product candidates or products, which in turn may delay, prevent or impair our development and commercialization efforts.

We have a letter agreement with IRIX Pharmaceuticals, Inc. ("IRIX"), a third-party manufacturer that we have used in the past, pursuant to which we agreed to negotiate a single source manufacturing agreement that included a right of first negotiation for the cGMP manufacture of HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third-party bids within 5%. The exclusive right to manufacture extends for five years after approval of an NDA for those compounds, and any agreement would provide that no minimum amounts would be specified until appropriate by forecast and that we and a commercialization partner would have the rights to contract with independent third parties that exceed IRIX's internal manufacturing capabilities or in the event that we or our commercialization partner determines for reasons of continuity of supply and security that such a need exists, provided that IRIX would supply no less than 65% of the product if it is able to provide this level of supply. Subsequent to the letter agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the letter agreement with respect to the single source manufacturing agreement, and if we were to enter into any such exclusive manufacturing agreement, there can be no assurance that IRIX will not assert a claim for right to manufacture roxadustat or that IRIX could manufacture roxadustat successfully and in accordance with applicable regulations for a commercial product and the specifications of our collaboration partners. In 2015, Patheon Pharmaceuticals Inc., a business unit of DPx Holdings B.V. ("Patheon"), acquired IRIX, and in 2017 ThermoFisher Scientific Inc. acquired Patheon.

If any third-party manufacturer terminates its engagement with us or fails to perform as agreed, we may be required to find replacement manufacturers, which would result in significant cost and delay to our development programs. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such third party or potential second source manufacturer. In any event, with any third-party manufacturer we expect to enter into technical transfer agreements and share our know-how with the third-party manufacturer, which can be time-consuming and may result in delays. These delays could result in a suspension or delay of marketing roxadustat.

Certain of the components of our product candidates are acquired from single-source suppliers and have been purchased without long-term supply agreements. The loss of any of these suppliers, or their failure to supply us with supplies of sufficient quantity and quality to complete our drug substance or finished drug product of acceptable quality and an acceptable price, would materially and adversely affect our business.

We do not have an alternative supplier of certain components of our product candidates. To date, we have used purchase orders for the supply of materials that we use in our product candidates. We may be unable to enter into long-term commercial supply arrangements with our vendors, or do so on commercially reasonable terms, which could have a material adverse impact upon our business. In addition, we currently rely on our contract manufacturers to purchase from third-party suppliers some of the materials necessary to produce our product candidates. We do not have direct control over the acquisition of those materials by our contract manufacturers. Moreover, we currently do not have any agreements for the commercial production of those materials.

The logistics of our supply chain, which include shipment of materials and intermediates from countries such as China and India add additional time and risk (including risk of loss) to the manufacture of our product candidates. While we have in the past maintained sufficient inventory of materials, active pharmaceutical ingredient ("API"), and drug product to meet our and our collaboration partners' needs for roxadustat to date, the lead time and regulatory approvals required to source from and into countries outside of the U.S. increase the risk of delay and potential shortages of supply.

Risks Related to Our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection and contractual arrangements to protect the intellectual property related to our technologies. We will only be able to protect our products and proprietary information and technology by preventing unauthorized use by third parties to the extent that our patents, trade secrets, and contractual position allow us to do so. Any disclosure to or misappropriation by third parties of our trade secrets or confidential information could compromise our competitive position. Moreover, we are involved in, have in the past been involved in, and may in the future be involved in legal or administrative proceedings involving our intellectual property initiated by third parties, and which proceedings can result in significant costs and commitment of management time and attention. As our product candidates continue in development, third parties may attempt to challenge the validity and enforceability of our patents and proprietary information and technologies.

We also are involved in, have in the past been involved in, and may in the future be involved in initiating legal or administrative proceedings involving the product candidates and intellectual property of our competitors. These proceedings can result in significant costs and commitment of management time and attention, and there can be no assurance that our efforts would be successful in preventing or limiting the ability of our competitors to market competing products.

Composition-of-matter patents relating to the API are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection not limited to any one method of use. Method-of-use patents protect the use of a product for the specified method(s), and do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. We rely on a combination of these and other types of patents to protect our product candidates, and there can be no assurance that our intellectual property will create and sustain the competitive position of our product candidates.

Biotechnology and pharmaceutical product patents involve highly complex legal and scientific questions and can be uncertain. Any patent applications that we own or license may fail to result in issued patents. Even if patents do successfully issue from our applications, third parties may challenge their validity or enforceability, which may result in such patents being narrowed, invalidated, or held unenforceable. Even if our patents and patent applications are not challenged by third parties, those patents and patent applications may not prevent others from designing around our claims and may not otherwise adequately protect our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, competitors with significantly greater resources could threaten our ability to commercialize our product candidates. Discoveries are generally published in the scientific literature well after their actual development, and patent applications in the U.S. and other countries are typically not published until 18 months after their filing, and in some cases are never published. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or patent applications, or that we or our licensors were the first to file for patent protection covering such inventions. Subject to meeting other requirements for patentability, for U.S. patent applications filed prior to March 16, 2013, the first to invent the claimed invention is entitled to receive patent protection for that invention while, outside the U.S., the first to file a patent application encompassing the invention is entitled to patent protection for the invention. The U.S. moved to a "first to file" system under the Leahy-Smith America Invents Act ("AIA"), effective March 16, 2013. This system also includes procedures for challenging issued patents and pending patent applications, which creates additional uncertainty. We may become involved in opposition or interference proceedings challenging our patents and patent applications or the patents and patent applications of others, and the outcome of any such proceedings are highly uncertain. An unfavorable outcome in any such proceedings could reduce the scope of or invalidate our patent rights, allow third parties to commercialize our technology and compete directly with us, or result in our inability to manufacture, develop or commercialize our product candidates without infringing the patent rights of others.

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In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to assign their inventions to us, and we require all of our employees, consultants, advisors and any third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how and other information and technology. Furthermore, the laws of some foreign countries, in particular, China, where we have operations, do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business and operations.

Intellectual property disputes with third parties and competitors may be costly and time consuming, and may negatively affect our competitive position.*

Our commercial success may depend on our avoiding infringement of the patents and other proprietary rights of third parties as well as on enforcing our patents and other proprietary rights against third parties. Pharmaceutical and biotechnology intellectual property disputes are characterized by complex, lengthy and expensive litigation over patents and other intellectual property rights. We may initiate or become party to or be threatened with future litigation or other proceedings regarding intellectual property rights with respect to our product candidates and competing products.

As our product candidates progress toward commercialization, we or our collaboration partners may be subject to patent infringement claims from third parties. We attempt to ensure that our product candidates do not infringe third-party patents and other proprietary rights. However, the patent landscape in competitive product areas is highly complex, and there may be patents of third parties of which we are unaware that may result in claims of infringement. Accordingly, there can be no assurance that our product candidates do not infringe proprietary rights of third parties, and parties making claims against us may seek and obtain injunctive or other equitable relief, which could potentially block further efforts to develop and commercialize our product candidates including roxadustat or pamrevlumab. Any litigation involving defense against claims of infringement, regardless of the merit of such claims, would involve substantial litigation expense and would be a substantial diversion of management time.

We may consider administrative proceedings and other means for challenging third-party patents and patent applications. An unfavorable outcome in any such challenge could require us to cease using the related technology and to attempt to license rights to it from the prevailing third party, which may not be available on commercially reasonable terms, if at all, in which case our business could be harmed.

We intend, if necessary, to vigorously enforce our intellectual property in order to protect the proprietary position of our product candidates, including roxadustat and pamrevlumab. In addition, our collaboration partners who have been granted licenses to our patents may also have rights related to enforcement of those patents. Active efforts to enforce our patents by us or by our partners may include litigation, administrative proceedings, or both, depending on the potential benefits that might be available from those actions and the costs associated with undertaking those efforts against third parties. We carefully review and monitor publicly available information regarding products that may be competitive with our product candidates and assert our intellectual property rights where appropriate. For example, we previously prevailed in an administrative challenge initiated by a major biopharmaceutical company regarding our intellectual property rights, maintaining our intellectual property in all relevant scope, and will continue to protect and enforce our intellectual property rights. In addition, our partner Astellas has recently initiated *quia timet* infringement actions against Akebia and GSK based on our specific patents in the United Kingdom in response to actions taken by Akebia and GSK against those patents, as further detailed below.

Third parties may also challenge our patents and patent applications, through interference, reexamination, *inter partes* review, and post-grant review proceedings before the U.S. Patent and Trademark Office ("USPTO") or through comparable proceedings in other territories. For example, Akebia and others have filed oppositions against certain European patents within our HIF anemia-related technologies patent portfolio. In three of these proceedings, for FibroGen European Patent Nos. 1463823, 1633333, and 2322155, the European Patent Office has handed down decisions unfavorable to FibroGen. In a fourth of these proceedings, the European Patent Office issued a decision favorable to FibroGen, maintaining FibroGen European Patent No. 2322153 in amended form. All of these decisions are currently under appeal, and these four patents are valid and enforceable pending resolution of the appeals. The ultimate outcomes of such proceedings remain uncertain, and ultimate resolution of the appeals may take two years or longer. In addition, Akebia recently filed oppositions against FibroGen European Patent Nos. 2289531 and 2298301. As mentioned above, Akebia and GSK have also initiated actions in the United Kingdom against the United Kingdom counterparts of each of these European Patent Nos. 2322153 and 2322155) with respect to its daprodustat product. Akebia is also pursuing invalidation actions against corresponding patents in Canada and in Japan. While we believe the ultimate outcome of all proceedings will be that these FibroGen patents will be upheld in relevant part, we note that narrowing or even revocation of any of these patents would not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia.

Oppositions have also recently been filed against our European Patent No. 2872488, which claims a crystalline form of roxadustat.

Furthermore, there is a risk that any public announcements concerning the status or outcomes of intellectual property litigation or administrative proceedings may adversely affect the price of our stock. If securities analysts or our investors interpret such status or outcomes as negative or otherwise creating uncertainty, our common stock price may be adversely affected.

Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.

Our reliance on third-party contractors to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our trade secrets and know-how. Despite the contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations in place with our collaboration partners. Despite our efforts to protect our trade secrets and other confidential information, a competitor's discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

We have an extensive worldwide patent portfolio. The cost of maintaining our patent protection is high and maintaining our patent protection requires continuous review and compliance in order to maintain worldwide patent protection. We may not be able to effectively maintain our intellectual property position throughout the major markets of the world.

The USPTO and foreign patent authorities require maintenance fees and payments as well as continued compliance with a number of procedural and documentary requirements. Noncompliance may result in abandonment or lapse of the subject patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance may result in reduced royalty payments for lack of patent coverage in a particular jurisdiction from our collaboration partners or may result in competition, either of which could have a material adverse effect on our business.

We have made, and will continue to make, certain strategic decisions in balancing costs and the potential protection afforded by the patent laws of certain countries. As a result, we may not be able to prevent third parties from practicing our inventions in all countries throughout the world, or from selling or importing products made using our inventions in and into the U.S. or other countries. Third parties may use our technologies in territories in which we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories which provide inadequate enforcement mechanisms, even if we have patent protection. Such third-party products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the U.S., and we may encounter significant problems in securing and defending our intellectual property rights outside the U.S.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries such as China, do not always favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop infringement of our patents, misappropriation of our trade secrets, or marketing of competing products in violation of our proprietary rights. In China, our intended establishment of significant operations will depend in substantial part on our ability to effectively enforce our intellectual property rights in that country. Proceedings to enforce our intellectual property rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, and could put our patents in these territories at risk of being invalidated or interpreted narrowly, or our patent applications at risk of not being granted, and could provoke third parties to assert claims against us. We may not prevail in all legal or other proceedings that we may initiate and, if we were to prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Intellectual property rights do not address all potential threats to any competitive advantage we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and intellectual property rights may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not
 covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- The prosecution of our pending patent applications may not result in granted patents.
- Granted patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid
 or unenforceable, as a result of legal challenges by our competitors.
- Patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product.
- Our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from
 patent infringement claims for such activities, as well as in countries in which we do not have patent rights, and may then use the
 information learned from such activities to develop competitive products for sale in markets where we intend to market our product
 candidates.

Roxadustat is considered a Class 2 substance on the 2019 World Anti-Doping Agency Prohibited List which could limit sales and increase security and distribution costs for us and our partners, particularly in China.

Roxadustat is considered a Class 2 substance on the World Anti-Doping Agency ("WADA") Prohibited List. There are enhanced security and distribution procedures we and our collaboration partners and third-party contractors will have to take to limit the risk of loss of product in the supply chain. As a result, our distribution, manufacturing and sales costs for roxadustat, as well as for our partners, will be increased which will reduce profitability. In addition, there is a risk of reduced sales due to patient access to this drug. This is particularly the case in China where we will not be able to sell roxadustat in private pharmacies due to the WADA classification. While private pharmacies only represent approximately 10% of the market in China, this will negatively affect sales and therefore the profitability of roxadustat and the Company as a whole.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold or used for research under the same or similar names, or similar mechanism of action or product class, but which are sold without proper licenses or approvals, and are often lower cost, lower quality, different potency, or have different ingredients or formulations, and have the potential to damage the reputation for quality and effectiveness of the genuine product. Such products may be used for indications or purposes that are not recommended or approved or for which there is no data or inadequate data with regard to safety or efficacy. Such products divert sales from genuine products. If counterfeit pharmaceuticals illegally sold or used for research result in adverse events or side effects to consumers, we may be associated with any negative publicity resulting from such incidents. Consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. In addition, the use of counterfeit products could be used in non-clinical or clinical studies, or could otherwise produce undesirable side effects or adverse events that may be attributed to our products as well, which could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for the commercialization of our product candidates.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. Except for roxadustat in China for patients on dialysis and not on dialysis, and Japan for patients on dialysis, we have not obtained regulatory approval for any product candidate, and it is possible that neither roxadustat nor pamrevlumab, nor any future product candidates we may discover, in-license or acquire and seek to develop in the future, will obtain regulatory approval in countries other than China and Japan.

Our product candidates could fail to receive regulatory approval from the FDA or other regulatory authorities for many reasons, including:

- disagreement over the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement over our interpretation of data from preclinical studies or clinical trials;
- disagreement over whether to accept efficacy results from clinical trial sites outside the U.S. where the standard of care is potentially different from that in the U.S.;
- the insufficiency of data collected from clinical trials of our present or future product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- disapproval of the manufacturing processes or facilities of either our manufacturing plant or third-party manufacturers with whom we contract for clinical and commercial supplies; or
- · changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

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The FDA or other regulatory authorities may require more information, including additional preclinical or clinical data to support approval, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program altogether. Even if we do obtain regulatory approval, our product candidates may be approved for fewer or more limited indications than we request, approval may be contingent on the performance of costly post-marketing clinical trials, or approval may require labeling that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS or other regulatory authorities may require the establishment of a similar strategy, that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we believe our current or planned clinical trials are successful, regulatory authorities may not agree that our completed clinical trials provide adequate data on safety or efficacy. Approval by one regulatory authority does not ensure approval by any other regulatory authority. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for regulatory approvals and even if we file we may not receive the necessary approvals to commercialize our product candidates in any market.

If our product candidates obtain marketing approval, we will be subject to more extensive healthcare laws, regulation and enforcement and our failure to comply with those laws could have a material adverse effect on our results of operations and financial condition.

If we obtain approval in the U.S. for any of our product candidates, the regulatory requirements applicable to our operations, in particular our sales and marketing efforts, will increase significantly with respect to our operations and the potential for civil and criminal enforcement by the federal government and the states and foreign governments will increase with respect to the conduct of our business. The laws that may affect our operations in the U.S. include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving,
 offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service
 reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes
 certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Patient Protection and Affordable Care Act ("PPACA"), which requires
 manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare and Medicaid Services
 ("CMS"), information related to payments and other transfers of value to physicians, other healthcare providers, and teaching
 hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family
 members;

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- foreign and state law equivalents of each of the above federal laws, such as the U.S. Foreign Corrupt Practices Act ("FCPA"), anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and
- the Trade Agreements Act ("TAA"), which requires that drugs sold to the U.S. Government must be manufactured in the U.S. or in TAA approved and designated countries. Drugs manufactured in countries not approved under the TAA, may not be sold to the U.S. without specific regulatory approval. We have little experience with this regulation and there is a risk that drugs made from Chinesemade API may not be sold to an entity of the U.S. such as the Veterans Health Administration ("VA") due to our inability to obtain regulatory approval. While there have been recent VA policy changes that appear to allow for sale of drugs from non-TAA approved countries, this policy may change or there may be additional policies or legislation that affect our ability to sell drug to the U.S. Government.

The scope of these laws and our lack of experience in establishing the compliance programs necessary to comply with this complex and evolving regulatory environment increases the risks that we may unknowingly violate the applicable laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results.

The impact of recent U.S. healthcare reform, its potential partial or full repeal, and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.

The commercial potential for our approved products could be affected by changes in healthcare spending and policy in the U.S. and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") altered Medicare coverage and payments for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. The MMA also provided authority for limiting the number of drugs that will be covered in any therapeutic class and as a result, we expect that there will be additional pressure to reduce costs. For example, the CMS in implementing the MMA has enacted regulations that reduced capitated payments to dialysis providers. These cost reduction initiatives and other provisions of the MMA could decrease the scope of coverage and the price that may be received for any approved dialysis products and could seriously harm our business and financial condition. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies have been enacted in many international markets which could similarly impact the commercial potential for our products.

Under the Medicare Improvements for Patients and Providers Act ("MIPPA"), a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by the CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage. It is unknown whether roxadustat, if approved in the U.S., will be included in the payment bundle. Under MIPPA, agents that have no IV equivalent in the bundle are currently expected to be excluded from the bundle until 2025. If roxadustat were included in the bundle, it may reduce the price that could be charged for roxadustat, and therefore potentially limit our profitability. Based on roxadustat's differentiated mechanism of action and therapeutic effects, and discussions with our collaboration partner, we currently believe that roxadustat might not be included in the bundle. If roxadustat is reimbursed outside of the bundle, it may potentially limit or delay market penetration of roxadustat.

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More recently, the PPACA was enacted in 2010 with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The PPACA, among other things, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D. In addition, other legislative changes have been proposed and adopted in the U.S. since the PPACA was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect on April 1, 2013.

It is likely that federal and state legislatures within the U.S. and foreign governments will continue to consider changes to existing healthcare legislation. We cannot predict the reform initiatives that may be adopted in the future or whether initiatives that have been adopted will be repealed or modified. The continuing efforts of the government, insurance companies, managed care organizations and other payors of healthcare services to contain or reduce costs of healthcare may adversely affect:

- the demand for any products that may be approved for sale;
- the price and profitability of our products;
- pricing, coverage and reimbursement applicable to our products;
- the ability to successfully position and market any approved product; and
- the taxes applicable to our pharmaceutical product revenues.

Some of the provisions of the PPACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the PPACA. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. Given these possibilities and others we may not anticipate, the full extent to which our business, results of operations and financial condition could be adversely affected by the recent proposed legislation and the Executive Order is uncertain. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our drugs.

Furthermore, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the regulatory approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent regulatory approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

We may not be able to conduct, or contract others to conduct, animal testing in the future, which could harm our research and development activities.

Certain laws and regulations relating to drug development require us to test our product candidates on animals before initiating clinical trials involving humans. Animal testing activities have been the subject of controversy and adverse publicity. Animal rights groups and other organizations and individuals have attempted to stop animal testing activities by pressing for legislation and regulation in these areas and by disrupting these activities through protests and other means. To the extent the activities of these groups are successful, our research and development activities may be interrupted or delayed.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could result in significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failure to:

- comply with FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or comparable foreign regulatory authorities;
- comply with manufacturing standards we have established;
- · comply with privacy laws protecting personal information;
- comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities;
- comply with the FCPA and other anti-bribery laws;
- report financial information or data accurately;
- or disclose unauthorized activities to us.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, delays in clinical trials, or serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could harm our business, results of operations, financial condition and cash flows, including through the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations applicable to our operations in the U.S. and foreign countries. These current or future laws and regulations may impair our research, development or manufacturing efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our International Operations

We are establishing international operations and seeking approval to commercialize our product candidates outside of the U.S., in particular in China, and a number of risks associated with international operations could materially and adversely affect our business.

We expect to be subject to a number of risks related with our international operations, many of which may be beyond our control. These risks include:

- different regulatory requirements for drug approvals in foreign countries;
- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain countries;

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- · changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems and different competitive drugs indicated to treat the indications for which our product candidates are being developed;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- · compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- compliance with the FCPA, and other anti-corruption and anti-bribery laws;
- U.S. and foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating costs and expenses and reduced revenues, and other
 obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- a reliance on CROs, clinical trial sites, principal investigators and other third parties that may be less experienced with clinical trials or have different methods of performing such clinical trials than we are used to in the U.S.;
- potential liability resulting from development work conducted by foreign distributors; and
- · business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. Refer to "Business - Government Regulation - Regulation in China" in our annual report on Form 10-K for the year ended December 31, 2018 for a discussion of the regulatory requirements that are applicable to our current and planned business activities in China. In recent years, the regulatory framework in China regarding the pharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes. Any such changes or amendments may result in increased compliance costs on our business or cause delays in or prevent the successful development or commercialization of our product candidates in China. For example, the NMPA recently adopted the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use guidelines, and accordingly imposed regulatory oversight earlier in our production process for roxadustat manufactured and sold in China. The change in regulatory starting material triggered an extension of the inspection to our contract manufacturer STA, which was successfully completed in October 2018. In addition, Chinese authorities have become increasingly vigilant in enforcing laws in the pharmaceutical industry, in some cases launching industry-wide investigations, oftentimes appearing to focus on foreign companies. The costs and time necessary to respond to an investigation can be material. Any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China.

We plan to use our own manufacturing facilities in China to produce roxadustat API, roxadustat drug product, and FG-5200 corneal implants. As an organization, we have limited experience in the construction, licensure, and operation of a manufacturing plant, and accordingly we cannot assure you we will be able to meet regulatory requirements to operate our plant and to sell our products.*

We have two manufacturing facilities in China, with one located in Beijing and the other in Cangzhou, Hebei. However, as an organization, we have limited experience licensing and operating commercial manufacturing facilities.

We will be obligated to comply with continuing cGMP requirements and there can be no assurance that we will maintain all of the appropriate licenses required to manufacture our product candidates for clinical and commercial use in China. In addition, we and our product suppliers must continually spend time, money and effort in production, record-keeping and quality assurance and appropriate controls in order to ensure that any products manufactured in our facilities meet applicable specifications and other requirements for product safety, efficacy and quality and there can be no assurance that our efforts will continue to be successful in meeting these requirements.

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We would require separate approval for the manufacture of FG-5200. In addition, we may convert the existing manufacturing process of FG-5200 to a semi-automated process, which may require us to show that implants from our new manufacturing process are comparable to the implants from our existing manufacturing process. There can be no assurance that we will successfully receive licensure and maintain approval for the manufacture of FG-5200, either of which would be expected to delay or preclude our ability to develop FG-5200 in China and may materially adversely affect our business and operations and prospects in China.

Manufacturing facilities in China are subject to periodic unannounced inspections by the NMPA and other regulatory authorities. We expect to depend on these facilities for our product candidates and business operations in China. Natural disasters or other unanticipated catastrophic events, including power interruptions, water shortages, storms, fires, earthquakes, terrorist attacks, government appropriation of our facilities, and wars, could significantly impair our ability to operate our manufacturing facilities. Certain equipment, records and other materials located in these facilities would be difficult to replace or would require substantial replacement lead time that would impact our ability to successfully commercialize our product candidates in China. The occurrence of any such event could materially and adversely affect our business, financial condition, results of operations, cash flows and prospects.

In addition to manufacturing, we are responsible for pharmacovigilance, medical affairs, and management of the third-party distribution logistics for roxadustat in China. We have no experience in these areas as a company, and accordingly we cannot assure you we will be able to meet regulatory requirements or operate in these capacities successfully.

We are responsible for commercial manufacturing, pharmacovigilance, medical affairs, and management of the third-party distribution logistics for roxadustat commercial activities in China. While we have been increasing our staffing in these areas, as a company, we have no experience managing or operating these functions for a commercial product and there can be no guarantee that we will do so efficiently or effectively. Mistakes or delays in these areas could limit our ability to successfully commercialize roxadustat in China, could limit our eventual market penetration, sales and profitability, and could subject us to significant liability in China.

We and our collaboration partner in China, AstraZeneca, may experience difficulties in successfully generating sales of roxadustat in China.*

We and AstraZeneca have a profit sharing arrangement with respect to roxadustat in China and any difficulties we may experience in generating sales will affect our bottom line. Difficulties may be related to our ability to obtain reasonable pricing, reimbursement, hospital listing, and tendering, or other difficulties related to distribution, marketing, and sales efforts in China. Sales of roxadustat in China may be limited due to the complex nature of the healthcare system, low average personal income, pricing controls, still developing infrastructure and potentially rapid competition from other products. The government has committed to updating the National Reimbursement Drug List ("NRDL") in 2019. Previous updates to the NRDL occurred in 2017 and 2009. In addition, there were also NRDL price negotiations in 2018 for oncology drugs. Admission to the NRDL depends on a number of factors, including on-market experience, scale of patient adoption, physician endorsement, cost-effectiveness and budget impact. Given that roxadustat was approved at the end of 2018, we may or may not qualify for the NRDL update in 2019. In particular, if we are unable to obtain reimbursement for roxadustat through the 2019 update to the NRDL, we may have to wait a substantial period of time before the reimbursement drug list is updated again. Without government reimbursement, many patients will not be able to afford roxadustat, since private commercial health insurance is rare, and our business and operations could be adversely affected. Therefore reimbursement and obtaining hospital listing is critical to roxadustat's near-term commercial success in China.

The market for treatment of anemia in CKD in China is highly competitive.*

Although we have now received approval for roxadustat for the treatment of anemia caused by CKD in dialysis patients and non-dialysis patients in China, it faces intense competition in the market for treatment of anemia in CKD. Roxadustat would compete with ESAs, which are offered by established multinational pharmaceutical companies such as Kyowa Hakko Kirin China Pharmaceutical Co., Ltd., Roche and Chinese pharmaceutical companies such as 3SBio Inc. and Di'ao Group Chengdu Diao Jiuhong Pharmaceutical Factory. Many of these competitors have substantially greater name recognition, scientific, financial, and marketing resources, as well as established distribution capabilities. Many of our competitors have more resources to develop or acquire, and more experience in developing or acquiring, new products and in creating market awareness for those products. Many of these competitors have significantly more experience than we have in navigating the Chinese regulatory framework regarding the development, manufacturing and marketing of drugs in China, as well as in marketing and selling anemia products in China. Additionally, we believe that most patients with anemia in CKD in China are currently being treated with traditional Chinese medicine, which is widely accepted and highly prevalent in China. Traditional Chinese medicine treatments are often oral and thus convenient and low-cost, and practitioners of traditional Chinese medicine are numerous and accessible in China. As a result, it may be difficult to persuade patients with anemia in CKD to switch from traditional Chinese medicine to roxadustat.

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The Chinese government is implementing a new "Two Invoices" regulation which could affect the way we structure our distributorship relationships in China for roxadustat.

The Chinese government is implementing new regulations that impact distribution of pharmaceutical products in China. These regulations generally require that at most two invoices may be issued throughout the distribution chain. Failure to comply with the "Two-Invoices" regulations would prevent us from accessing the market in China. We are planning on modifying the distribution responsibilities under the China Agreement between AstraZeneca and FibroGen such that FibroGen would engage distributors and a third-party logistics provider, and both companies will work together to manage the distribution network. FibroGen China Anemia Holdings, Ltd ("FibroGen China") has never managed distribution of pharmaceutical products, and this new distribution structure may impose higher costs or limit or delay our ability to sell products to our principal customers, and may limit the near term sales of our products.

There is no assurance that roxadustat will be included in the Medical Insurance Catalogs.

Eligible participants in the national basic medical insurance program in China, which consists of mostly urban residents, are entitled to reimbursement from the social medical insurance fund for up to the entire cost of medicines that are included in the Medical Insurance Catalogs. Refer to "Business - Government Regulation - Regulation in China" in our annual report on Form 10-K for the year ended December 31, 2018. We believe that the inclusion of a drug in the Medical Insurance Catalogs can substantially improve the sales of a drug in China. The Ministry of Labor and Social Security in China ("MLSS") together with other government authorities, select medicines to be included in the Medical Insurance Catalogs based on a variety of factors, including treatment requirements, frequency of use, effectiveness and price. The MLSS also occasionally removes medicines from such catalogs. There can be no assurance that roxadustat will be included, and once included, remain in the Medical Insurance Catalogs. The exclusion or removal of roxadustat from the Medical Insurance Catalogs may materially and adversely affect sales of roxadustat.

Even if FG-5200 can be manufactured successfully and achieve regulatory approval, we may not achieve commercial success.

We have not yet received a license to manufacture FG-5200 in our Beijing manufacturing facility or at scale, and we will have to show that FG-5200 produced in our China manufacturing facility meets the applicable regulatory requirements. There can be no assurance that we can meet these requirements or that FG-5200 can be approved for development, manufacture and sale in China.

Even if we are able to manufacture and develop FG-5200 as a medical device in China, the size and length of any potential clinical trials required for approval are uncertain and we are unable to predict the time and investment required to obtain regulatory approval. Moreover, even if FG-5200 can be successfully developed for approval in China, our product candidate would require extensive training and investment in assisting physicians in the use of FG-5200.

The retail prices of any product candidates that we develop may be subject to control, including periodic downward adjustment, by Chinese government authorities.

The price for pharmaceutical products is highly regulated in China, both at the national and provincial level. Price controls may reduce prices to levels significantly below those that would prevail in less regulated markets or limit the volume of products that may be sold, either of which may have a material and adverse effect on potential revenues from sales of roxadustat in China. Moreover, the process and timing for the implementation of price restrictions is unpredictable, which may cause potential revenues from the sales of roxadustat to fluctuate from period to period.

If our planned business activities in China fall within a restricted category under the China Catalog for Guidance for Foreign Investment, we will need to operate in China through a variable interest entity ("VIE") structure.

The China Catalog for Guidance for Foreign Investment sets forth the industries and sectors that the Chinese government encourages and restricts with respect to foreign investment and participation. The Catalog for Guidance for Foreign Investment is subject to revision from time to time by the China Ministry of Commerce. While we currently do not believe the development and marketing of roxadustat falls within a restricted category under the Catalog for Guidance for Foreign Investment, if roxadustat does fall under such a restricted category, we will need to operate in China through a VIE structure. A VIE structure involves a wholly foreign-owned enterprise that would control and receive the economic benefits of a domestic Chinese company through various contractual relationships. Such a structure would subject us to a number of risks that may have an adverse effect on our business, including that the Chinese government may determine that such contractual arrangements do not comply with applicable regulations, Chinese tax authorities may require us to pay additional taxes, shareholders of our VIEs may have potential conflicts of interest with us, and we may lose the ability to use and enjoy assets held by our VIEs that are important to the operations of our business if such entities go bankrupt or become subject to dissolution or liquidation proceedings. VIE structures in China have come under increasing scrutiny from accounting firms and the Securities and Exchange Commission ("SEC") staff. If we do attempt to use a VIE structure and are unsuccessful in structuring it so as to qualify as a VIE, we would not be able to consolidate the financial statements of the VIE with our financial statements, which could have a material adverse effect on our operating results and financial condition.

FibroGen Beijing would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.*

We plan to conduct all of our business in China through FibroGen China and FibroGen Beijing. We may rely on dividends and royalties paid by FibroGen Beijing for a portion of our cash needs, including the funds necessary to service any debt we may incur and to pay our operating costs and expenses. The payment of dividends by FibroGen Beijing is subject to limitations. Regulations in China currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in China. FibroGen Beijing is not permitted to distribute any profits until losses from prior fiscal years have been recouped and in any event must maintain certain minimum capital requirements. FibroGen Beijing is also required to set aside at least 10.0% of its after-tax profit based on Chinese accounting standards each year to its statutory reserve fund until the cumulative amount of such reserves reaches 50.0% of its registered capital. Statutory reserves are not distributable as cash dividends. In addition, if FibroGen Beijing incurs debt on its own behalf in the future, the agreements governing such debt may restrict its ability to pay dividends or make other distributions to us. As of September 30, 2019, approximately \$6.9 million of our cash and cash equivalents is held in China.

Any capital contributions from us to FibroGen Beijing must be approved by the Ministry of Commerce in China, and failure to obtain such approval may materially and adversely affect the liquidity position of FibroGen Beijing.

The Ministry of Commerce in China or its local counterpart must approve the amount and use of any capital contributions from us to FibroGen Beijing, and there can be no assurance that we will be able to complete the necessary government registrations and obtain the necessary government approvals on a timely basis, or at all. If we fail to do so, we may not be able to contribute additional capital to fund our Chinese operations, and the liquidity and financial position of FibroGen Beijing may be materially and adversely affected.

We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.*

Most of our product sales will occur in local Chinese currency and our operating results will be subject to volatility from currency exchange rate fluctuations. To date, we have not hedged against the risks associated with fluctuations in exchange rates and, therefore, exchange rate fluctuations could have an adverse impact on our future operating results. Changes in value of the Renminbi against the U.S. dollar, Euro and other currencies is affected by, among other things, changes in China's political and economic conditions. Currently, the Renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. Any significant currency exchange rate fluctuations may have a material adverse effect on our business and financial condition.

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In addition, the Chinese government imposes controls on the convertibility of the Renminbi into foreign currencies and the remittance of foreign currency out of China for certain transactions. Shortages in the availability of foreign currency may restrict the ability of FibroGen Beijing to remit sufficient foreign currency to pay dividends or other payments to us, or otherwise satisfy their foreign currency-denominated obligations. Under existing Chinese foreign exchange regulations, payments of current account items, including profit distributions, interest payments and balance of trade, can be made in foreign currencies without prior approval from the State Administration of Foreign Exchange ("SAFE") by complying with certain procedural requirements. However, approval from SAFE or its local branch is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The Chinese government may also at its discretion restrict access in the future to foreign currencies for current account transactions. If the foreign exchange control system prevents us from obtaining sufficient foreign currency to satisfy our operational requirements, our liquidity and financial position may be materially and adversely affected.

Because FibroGen Beijing's funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen Beijing deposits its funds could adversely affect our business.

Banks and other financial institutions in China do not provide insurance for funds held on deposit. As a result, in the event of a bank failure, FibroGen Beijing may not have access to funds on deposit. Depending upon the amount of money FibroGen Beijing maintains in a bank that fails, its inability to have access to cash could materially impair its operations.

We may be subject to tax inefficiencies associated with our offshore corporate structure.*

The tax regulations of the U.S. and other jurisdictions in which we operate are extremely complex and subject to change. New laws, new interpretations of existing laws, such as the Base Erosion Profit Shifting project initiated by the Organization for Economic Co-operation and Development, and any legislation proposed by the relevant taxing authorities, or limitations on our ability to structure our operations and intercompany transactions may lead to inefficient tax treatment of our revenue, profits, royalties, and distributions, if any are achieved.

In addition, we and our foreign subsidiaries have various intercompany transactions. We may not be able to obtain certain benefits under relevant tax treaties to avoid double taxation on certain transactions among our subsidiaries. If we are not able to avail ourselves to the tax treaties, we could be subject to additional taxes, which could adversely affect our financial condition and results of operations.

On December 22, 2017, the U.S. enacted the Tax Cuts and Jobs Act ("Tax Act") that instituted fundamental changes to the taxation of multinational corporations. The Tax Act includes changes to the taxation of foreign earnings by implementing a dividend exemption system, expansion of the current anti-deferral rules, a minimum tax on low-taxed foreign earnings and new measures to deter base erosion. The Tax Act also includes a permanent reduction in the corporate tax rate to 21%, repeal of the corporate alternative minimum tax, expensing of capital investment, and limitation of the deduction for interest expense. Furthermore, as part of the transition to the new tax system, a one-time transition tax is imposed on a U.S. shareholder's historical undistributed earnings of foreign affiliates. There have been developing interpretations of the provisions of the Tax Act, including changes and issuance of new U.S. Treasury regulations, administrative interpretations, or court decisions since its inception. As regulations and guidance evolve with respect to the Tax Act, we continue to examine the impact to our business, which could have a material adverse effect on our business, results of operations or financial condition.

Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.

We seek to protect the products and technology that we consider important to our business by pursuing patent applications in China and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. We note that the filing of a patent application does not mean that we will be granted a patent, or that any patent eventually granted will be as broad as requested in the patent application or will be sufficient to protect our technology. There are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications not to be granted, including known or unknown prior art, deficiencies in the patent application, or lack of originality of the technology. Furthermore, the terms of our patents are limited. The patents we hold and the patents that may be granted from our currently pending patent applications have, absent any patent term adjustment or extension, a twenty-year protection period starting from the date of application.

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Intellectual property rights and confidentiality protections in China may not be as effective as those in the U.S. or other countries for many reasons, including lack of procedural rules for discovery and evidence, low damage awards, and lack of judicial independence. Implementation and enforcement of China intellectual property laws have historically been deficient and ineffective and may be hampered by corruption and local protectionism. Policing unauthorized use of proprietary technology is difficult and expensive, and we may need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability and validity of our proprietary rights or those of others. The experience and capabilities of China courts in handling intellectual property litigation varies and outcomes are unpredictable. An adverse determination in any such litigation could materially impair our intellectual property rights and may harm our business.

We are subject to laws and regulations governing corruption, which will require us to develop, maintain, and implement costly compliance programs.

We must comply with a wide range of laws and regulations to prevent corruption, bribery, and other unethical business practices, including the FCPA, anti-bribery and anti-corruption laws in other countries, particularly China. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

Anti-bribery laws prohibit us, our employees, and some of our agents or representatives from offering or providing any personal benefit to covered government officials to influence their performance of their duties or induce them to serve interests other than the missions of the public organizations in which they serve. Certain commercial bribery rules also prohibit offering or providing any personal benefit to employees and representatives of commercial companies to influence their performance of their duties or induce them to serve interests other than their employers. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with these anti-bribery laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the anti-bribery laws present particular challenges in the pharmaceutical industry because in many countries including China, hospitals are state-owned or operated by the government, and doctors and other hospital employees are considered foreign government officials. Furthermore, in certain countries (China in particular), hospitals and clinics are permitted to sell pharmaceuticals to their patients and are primary or significant distributors of pharmaceuticals. Certain payments to hospitals in connection with clinical studies, procurement of pharmaceuticals and other work have been deemed to be improper payments to government officials that have led to vigorous anti-bribery law enforcement actions and heavy fines in multiple jurisdictions, particularly in the U.S. and China.

It is not always possible to identify and deter violations, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

In the pharmaceutical industry, corrupt practices include, among others, acceptance of kickbacks, bribes or other illegal gains or benefits by the hospitals and medical practitioners from pharmaceutical manufacturers, distributors or their third-party agents in connection with the prescription of certain pharmaceuticals. If our employees, affiliates, distributors or third-party marketing firms violate these laws or otherwise engage in illegal practices with respect to their sales or marketing of our products or other activities involving our products, we could be required to pay damages or heavy fines by multiple jurisdictions where we operate, which could materially and adversely affect our financial condition and results of operations. The Chinese government has also sponsored anti-corruption campaigns from time to time, which could have a chilling effect on any future marketing efforts by us to new hospital customers. There have been recent occurrences in which certain hospitals have denied access to sales representatives from pharmaceutical companies because the hospitals wanted to avoid the perception of corruption. If this attitude becomes widespread among our potential customers, our ability to promote our products to hospitals may be adversely affected.

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As we expand our operations in China and other jurisdictions internationally, we will need to increase the scope of our compliance programs to address the risks relating to the potential for violations of the FCPA and other anti-bribery and anti-corruption laws. Our compliance programs will need to include policies addressing not only the FCPA, but also the provisions of a variety of anti-bribery and anti-corruption laws in multiple foreign jurisdictions, including China, provisions relating to books and records that apply to us as a public company, and include effective training for our personnel throughout our organization. The creation and implementation of anti-corruption compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. Violation of the FCPA and other anti-corruption laws can result in significant administrative and criminal penalties for us and our employees, including substantial fines, suspension or debarment from government contracting, prison sentences, or even the death penalty in extremely serious cases in certain countries. The SEC also may suspend or bar us from trading securities on U.S. exchanges for violation of the FCPA's accounting provisions. Even if we are not ultimately punished by government authorities, the costs of investigation and review, distraction of our personnel, legal defense costs, and harm to our reputation could be substantial and could limit our profitability or our ability to develop or commercialize our product candidates. In addition, if any of our competitors are not subject to the FCPA, they may engage in practices that will lead to their receipt of preferential treatment from foreign hospitals and enable them to secure business from foreign hospitals in ways that are unavailable to us.

Uncertainties with respect to the China legal system could have a material adverse effect on us.

The legal system of China is a civil law system primarily based on written statutes. Unlike in a common law system, prior court decisions may be cited for reference but are not binding. Because the China legal system continues to rapidly evolve, the interpretations of many laws, regulations and rules are not always uniform and enforcement of these laws, regulations and rules involve uncertainties, which may limit legal protections available to us. Moreover, decision makers in the China judicial system have significant discretion in interpreting and implementing statutory and contractual terms, which may render it difficult for FibroGen Beijing to enforce the contracts it has entered into with our business partners, customers and suppliers. Different government departments may have different interpretations of certain laws and regulations, and licenses and permits issued or granted by one government authority may be revoked by a higher government authority at a later time. Navigating the uncertainty and change in the China legal system will require the devotion of significant resources and time, and there can be no assurance that our contractual and other rights will ultimately be enforced.

Changes in China's economic, political or social conditions or government policies could have a material adverse effect on our business and operations.*

Chinese society and the Chinese economy continue to undergo significant change. Changes in the regulatory structure, regulations, and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy, but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the regulatory structure and structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes and structural changes, any of which could materially and adversely affect FibroGen Beijing's development and commercialization timelines, liquidity, access to capital, and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China. In addition, the changing government regulations and policies could result in delays and cost increases to our development, manufacturing, approval, and commercialization timelines in China.

Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may materially and adversely affect our business, financial condition and results of operations.

We are subject to China Labor Contract Law, which provides strong protections for employees and imposes many obligations on employers. The Labor Contract Law places certain restrictions on the circumstances under which employers may terminate labor contracts and require economic compensation to employees upon termination of employment, among other things. In addition, companies operating in China are generally required to contribute to labor union funds and the mandatory social insurance and housing funds. Any failure by us to comply with Chinese labor and social insurance laws may subject us to late fees, fines and penalties, or cause the suspension or termination of our ability to conduct business in China, any of which could have a material and adverse effect on business, results of operations and prospects.

Recent developments relating to the United Kingdom's referendum vote in favor of leaving the EU could adversely affect us.

The United Kingdom held a referendum on June 23, 2016 in which a majority voted for the United Kingdom's withdrawal from the EU, commonly referred to as "Brexit". As a result of this vote, negotiations are expected to commence to determine the terms of the United Kingdom's withdrawal from the EU as well as its relationship with the EU going forward, including the terms of trade between the United Kingdom and the EU. The effects of the United Kingdom's withdrawal from the EU, and the perceptions as to its impact, are expected to be far-reaching and may adversely affect business activity and economic conditions in Europe and globally and could continue to contribute to instability in global financial markets, including foreign exchange markets. The United Kingdom's withdrawal from the EU could also have the effect of disrupting the free movement of goods, services and people between the United Kingdom and the EU and could also lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which EU laws to replace or replicate, including laws that could impact our ability, or our collaborator's ability in the case of roxadustat, to obtain approval of our products or sell our products in the United Kingdom. However, the full effects of such withdrawal are uncertain and will depend on any agreements the United Kingdom may make to retain access to EU markets. Lastly, as a result of the United Kingdom's withdrawal from the EU, other European countries may seek to conduct referenda with respect to their continuing membership with the EU. Given these possibilities and others we may not anticipate, as well as the lack of comparable precedent, the full extent to which our business, results of operations and financial condition could be adversely affected by the United Kingdom's withdrawal from the EU is uncertain.

Risks Related to the Operation of Our Business

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, commercialization and administration capabilities or contract with third parties to provide these capabilities for us. As our operations expand and we continue to undertake the efforts and expense to operate as a public reporting company, we expect that we will need to increase the responsibilities on members of management in order to manage any future growth effectively. Our failure to accomplish any of these steps could prevent us from successfully implementing our strategy and maintaining the confidence of investors in our Company.

Loss of senior management and key personnel, including the recent passing of our founder, chairman and chief executive officer, could adversely affect our ability to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.*

We are highly dependent on members of our senior management team, in particular our chief executive officer. On August 26, 2019, we announced the passing of Thomas B. Neff, our founder, chairman and chief executive officer. It was concurrently announced that James Schoeneck, a longtime member of our Board of Directors, was appointed as interim chief executive officer and that the Board of Directors would pursue the search for a permanent chief executive officer. The transitions in our executive team over the next year or more may be disruptive to our operations. The loss of the services of Mr. Neff and the potential delay with finding a permanent CEO could significantly negatively impact the development and commercialization of our product candidates, our existing collaborative relationships, and our ability to successfully implement our business strategy.

Recruiting and retaining qualified commercial, development, scientific, clinical, and manufacturing personnel are and will continue to be critical to our success, particularly as we expand our commercialization operations. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

There is also significant competition, in particular in the San Francisco Bay Area, for the hiring of experienced and qualified personnel, which increases the importance of retention of our existing personnel. If we are unable to continue to attract and retain personnel with the quality and experience applicable to our product candidates, our ability to pursue our strategy will be limited and our business and operations would be adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing, manufacturing and commercialization of our product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under state consumer protection acts. If we are unable to obtain insurance coverage at levels that are appropriate to maintain our business and operations, or if we are unable to successfully defend ourselves against product liability claims, we may incur substantial liabilities or otherwise cease operations. Product liability claims may result in:

- · termination of further development of unapproved product candidates or significantly reduced demand for any approved products;
- material costs and expenses to defend the related litigation;
- a diversion of time and resources across the entire organization, including our executive management;
- product recalls, withdrawals or labeling restrictions;
- · termination of our collaboration relationships or disputes with our collaboration partners; and
- · reputational damage negatively impacting our other product candidates in development.

If we fail to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, we may not be able to continue to develop our product candidates. We maintain product liability insurance in a customary amount for the stage of development of our product candidates. Although we believe that we have sufficient coverage based on the advice of our third-party advisors, there can be no assurance that such levels will be sufficient for our needs. Moreover, our insurance policies have various exclusions, and we may be in a dispute with our carrier as to the extent and nature of our coverage, including whether we are covered under the applicable product liability policy. If we are not able to ensure coverage or are required to pay substantial amounts to settle or otherwise contest the claims for product liability, our business and operations would be negatively affected.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, collaboration partners, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We upgraded our disaster and data recovery capabilities in June 2017, however, to the extent that any disruption or security breach, in particular with our partners' operations, results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and it could result in a material disruption and delay of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

We depend on sophisticated information technology systems to operate our business and a cyber-attack or other breach of these systems could have a material adverse effect on our business.

We rely on information technology systems to process, transmit and store electronic information in our day-to-day operations. The size and complexity of our information technology systems makes them vulnerable to a cyber-attack, malicious intrusion, breakdown, destruction, loss of data privacy or other significant disruption. While we have recently upgraded our disaster data recovery program, a successful attack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyber-attacks are becoming more sophisticated and frequent. We have invested in our systems and the protection and recoverability of our data to reduce the risk of an intrusion or interruption, and we monitor and test our systems on an ongoing basis for any current or potential threats. There can be no assurance that these measures and efforts will prevent future interruptions or breakdowns. If we fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to these systems, we could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating costs and expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows.

Our headquarters and data storage facilities are located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business, results of operations and financial condition.

We and some of the third-party service providers on which we depend for various support functions, such as data storage, are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires.

We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, or otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place are unlikely to provide adequate protection in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above your purchase price.

In general, pharmaceutical, biotechnology and other life sciences company stocks have been highly volatile in the current market. The volatility of pharmaceutical, biotechnology and other life sciences company stocks is sometimes unrelated to the operating performance of particular companies and biotechnology and life science companies stocks often respond to trends and perceptions rather than financial performance. In particular, the market price of shares of our common stock could be subject to wide fluctuations in response to the following factors:

- results of clinical trials of our product candidates, including roxadustat and pamrevlumab;
- the timing of the release of results of and regulatory updates regarding our clinical trials;
- the level of expenses related to any of our product candidates or clinical development programs;
- · results of clinical trials of our competitors' products;
- safety issues with respect to our product candidates or our competitors' products;
- regulatory actions with respect to our product candidates and any approved products or our competitors' products;
- fluctuations in our financial condition and operating results, which will be significantly affected by the manner in which we recognize revenue from the achievement of milestones under our collaboration agreements;
- adverse developments concerning our collaborations and our manufacturers;
- the termination of a collaboration or the inability to establish additional collaborations;
- the publication of research reports by securities analysts about us or our competitors or our industry or negative recommendations or withdrawal of research coverage by securities analysts;
- · the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- the ineffectiveness of our internal controls;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;

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- additions and departures of key personnel;
- announced strategic decisions by us or our competitors;
- changes in legislation or other regulatory developments affecting our product candidates or our industry;
- · fluctuations in the valuation of the biotechnology industry and particular companies perceived by investors to be comparable to us;
- sales of our common stock by us, our insiders or our other stockholders;
- · speculation in the press or investment community;
- announcement or expectation of additional financing efforts;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- changes in accounting principles;
- · activities of the government of China, including those related to the pharmaceutical industry as well as industrial policy generally;
- performance of other U.S. publicly traded companies with significant operations in China;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters such as earthquakes and other calamities;
- changes in market conditions for biopharmaceutical stocks;
- changes in general market and economic conditions; and
- the other factors described in this "Risk Factors" section.

As a result of fluctuations caused by these and other factors, comparisons of our operating results across different periods may not be accurate indicators of our future performance. Any fluctuations that we report in the future may differ from the expectations of market analysts and investors, which could cause the price of our common stock to fluctuate significantly. Moreover, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources and could also require us to make substantial payments to satisfy judgments or to settle litigation.

We have broad discretion in the use of the remaining net proceeds from our underwritten public offerings of common stock completed on April 11, 2017 (the "April 2017 Offering") and August 24, 2017 (the "August 2017 Offering") and may not use them effectively.

The net proceeds from the April 2017 Offering is intended to be used to fund the expansion of product development in China, including developing roxadustat in additional indications beyond CKD, manufacturing and commercialization activities, as well as for general corporate purposes. The net proceeds from the August 2017 Offering is intended to be used to fund the expansion of product development, including our development of pamrevlumab through Phase 3 trials, manufacturing and commercialization activities, as well as for general corporate purposes. These general corporate purposes, may include, among other things, funding research and development, clinical trials, vendor payables, potential regulatory submissions, hiring additional personnel and capital expenditures. However, we have no current commitments or obligations to use the net proceeds in the manner described above. Our management has broad discretion in the application of the remaining net proceeds from the April 2017 Offering and the August 2017 Offering, and could spend the remaining net proceeds in ways our stockholders may not agree with or that fails to improve our business or enhance the value of our common stock. The failure by our management to use these funds effectively could result in financial losses that could harm our business, cause the price of our common stock to decline and delay the development of our product candidates.

If securities or industry analysts do not continue to publish research or reports about our business, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock, our stock price would likely decline. If one or more of these analysts cease coverage of our Company or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.*

As of October 31, 2019, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 28.00% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date and shares issuable upon settlement of restricted stock units that will vest within 60 days after such date. This percentage is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G, if any, filed with the SEC, which information may not be accurate as of April 30, 2019. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. The interests of this group may differ from those of other stockholders and they may vote their shares in a way that is contrary to the way other stockholders vote their shares. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

Additional remedial measures that may be imposed in the proceedings instituted by the SEC against five China based accounting firms, including the Chinese affiliate of our independent registered public accounting firm, could result in our consolidated financial statements being determined to not be in compliance with the requirements of the Exchange Act.

In late 2012, the SEC commenced administrative proceedings under Rule 102(e) of its Rules of Practice and also under the Sarbanes-Oxley Act of 2002 against the Chinese affiliates of the "big four" accounting firms, including PricewaterhouseCoopers Zhong Tian CPAs Limited, the Chinese affiliate of our independent registered public accounting firm. The Rule 102(e) proceedings initiated by the SEC relate to these firms' failure to produce documents, including audit work papers, in response to the request of the SEC pursuant to Section 106 of the Sarbanes-Oxley Act of 2002, as the auditors located in China are not in a position lawfully to produce documents directly to the SEC because of restrictions under Chinese law and specific directives issued by the China Securities Regulatory Commission ("CSRC"). The issues raised by the proceedings are not specific to our auditors or to us.

In January 2014, an administrative law judge reached an initial decision that the Chinese affiliates of the "big four" accounting firms should be barred from practicing before the SEC for a period of six months. In February 2015, the Chinese affiliates of the "big four" accounting firms each agreed to a censure and to pay a fine to the SEC to settle the dispute and avoid suspension of their ability to practice before the SEC and audit U.S.-listed companies. The settlement required the firms to follow detailed procedures and to seek to provide the SEC with access to Chinese firms' audit documents via the CSRC. If future document productions fail to meet specified criteria, the SEC retains authority to impose a variety of additional remedial measures on the firms depending on the nature of the failure.

We cannot predict if the SEC will further review the four firms' compliance with specified criteria or if such further review would result in the SEC imposing additional penalties such as suspensions or commencing any further administrative proceedings. Although it does not play a substantial role (as defined under PCAOB standards) in the audit of our consolidated financial statements, if PricewaterhouseCoopers Zhong Tian CPAs Limited were denied, temporarily, the ability to practice before the SEC, our ability to produce audited consolidated financial statements for our Company could be affected and we could be determined not to be in compliance with the requirements of the Exchange Act. Such a determination could ultimately lead to the delisting of our shares from the Nasdaq Global Select Market or deregistration from the SEC, or both, which would substantially reduce or effectively terminate the trading of our stock.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our business, results of operations, financial condition and cash flows and future prospects.

While we currently have no specific plans to acquire any other businesses, we may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our present or future product candidates and business or otherwise offer opportunities for our Company. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our existing stockholders' percentage of ownership;
- · incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

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We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- · problems integrating the purchased business, products or technologies, or employees or other assets of the acquisition target;
- · increases to our expenses;
- disclosed or undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- reprioritization of our development programs and even cessation of development and commercialization of our current product candidates;
- · harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current directors or management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a
 majority of the total number of directors;
- · prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed prior to the end of their term only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a
 quorum;
- require a supermajority vote of the holders of our common stock or the majority vote of our board of directors to amend our bylaws;
 and
- require a supermajority vote of the holders of our common stock to amend the classification of our board of directors into three classes and to amend certain other provisions of our certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

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Moreover, because we are incorporated in Delaware, we are governed by certain anti-takeover provisions under Delaware law which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. We are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Changes in our tax provision or exposure to additional tax liabilities could adversely affect our earnings and financial condition.*

As a multinational corporation, we are subject to income taxes in the U.S. and various foreign jurisdictions. Significant judgment is required in determining our global provision for income taxes and other tax liabilities. In the ordinary course of a global business, there are intercompany transactions and calculations where the ultimate tax determination is uncertain. Our income tax returns are subject to audits by tax authorities. Although we regularly assess the likelihood of adverse outcomes resulting from these examinations to determine our tax estimates, a final determination of tax audits or tax disputes could have an adverse effect on our results of operations and financial condition.

We are also subject to non-income taxes, such as payroll, sales, use, value-added, net worth, property, gross receipts, and goods and services taxes in the U.S., state and local, and various foreign jurisdictions. We are subject to audit and assessments by tax authorities with respect to these non-income taxes and may have exposure to additional non-income tax liabilities, which could have an adverse effect on our results of operations and financial condition.

In addition, our judgment in providing for the possible impact of the Tax Act remains subject to developing interpretations of the provisions of the Tax Act. As regulations and guidance evolve with respect to the Tax Act, we continue to examine the impact to our tax provision or exposure to additional tax liabilities, which could have a material adverse effect on our business, results of operations or financial condition.

Our amended and restated certificate of incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in our product candidates and maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

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ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS.

Use of Proceeds from Initial Public Offering of Common Stock

On November 13, 2014, our Registration Statement on Form S-1, as amended (Reg. Nos. 333-199069 and 333-200189) was declared effective in connection with the initial public offering of our common stock. There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on November 14, 2014.

On May 2, 2019, we issued an aggregate of 4,430 shares of our common stock to a warrant holder who exercised an outstanding warrant to purchase our common stock at an exercise price of \$15.00 per share, for an aggregation consideration of \$66,456. This issuance was exempt from registration under Section 4(2) of the Securities Act of 1933, as amended, as sales of securities not involving any public offering.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES.

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES.

Not applicable.

ITEM 5. OTHER INFORMATION.

None.

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ITEM 6. EXHIBITS

Exhibit	_		Incorporation By Reference		
Number	Exhibit Description	Form	SEC File No.	Exhibit	Filing Date
3.1	Amended and Restated Certificate of Incorporation of FibroGen, Inc.	8-K	001-36740	3.1	11/21/2014
3.2	Amended and Restated Bylaws of FibroGen, Inc.	S-1/A	333-199069	3.4	10/23/2014
4.1	Form of Common Stock Certificate.	8-K	001-36740	4.1	11/21/2014
4.5	Common Stock Purchase Agreement by and between FibroGen, Inc.	S-1/A	333-199069	4.17	10/24/2014
	and AstraZeneca AB, dated as of October 20, 2014.				
4.6	Shareholders' Agreement by and among FibroGen International	10-Q	001-36740	4.6	11/8/2017
	(Cayman) Limited and certain of its shareholders, dated as of September 8, 2017.				
10.6*+	FibroGen, Inc. Non-Employee Director Compensation Policy, as amended.	-	-	-	-
10.7*+	Offer Letter, by and between FibroGen, Inc. and James Schoeneck, dated September 18, 2019.	-	-	-	-
31.1*	Certification of Chief Executive Officer, as required by Rule 13a-14(a)	-	-	-	-
	or Rule 15d-14(a).				
31.2*	Certification of Chief Financial Officer, as required by Rule 13a-14(a)	-	-	-	-
	<u>or Rule 15d-14(a).</u>				
32.1*	Certification of Principal Executive Officer and Principal Financial	-	-	-	-
	Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C.				
	\$1350 (1 Chapter 65 of Title 18 of the Officer States Code (18 O.S.C.				
101.INS	Inline XBRL Instance Document	_	-	_	_
101.SCH	Inline XBRL Taxonomy Extension Schema Document	_	-	-	_
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	_	-	-	_
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	-	-	-	-
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	-	-	-	-
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	-	-	-	-
104	Cover Page Interactive Data File (formatted as inline XBRL with	-	-	-	-
	applicable taxonomy extension information contained in Exhibits				
	101.*)				
* E31. J 1.					

^{*} Filed herewith

⁺ Indicates a management contract or compensatory plan

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

Dated: November 12, 2019

Dated: November 12, 2019

FibroGen, Inc.

By: /s/ James Schoeneck

James Schoeneck Interim Chief Executive Officer (Principal Executive Officer)

By: /s/ Pat Cotroneo

Pat Cotroneo

Senior Vice President, Finance and Chief Financial Officer (Principal Financial and Accounting Officer)

Exhibit 31.1

CERTIFICATION

- I, James Schoeneck, certify that;
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 12, 2019

/s/ James Schoeneck
James Schoeneck
Interim Chief Executive Officer

(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

- I, Pat Cotroneo, certify that;
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 12, 2019

/s/ Pat Cotroneo

Pat Cotroneo Senior Vice President, Finance and Chief Financial Officer (Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended ("Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), James Schoeneck, Interim Chief Executive Officer of FibroGen, Inc. ("the Company"), and Pat Cotroneo, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

- 1. The Company's Quarterly Report on Form 10-Q for the period ended September 30, 2019, to which this Certification is attached as Exhibit 32.1 ("Periodic Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and
- 2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: November 12, 2019

IN WITNESS WHEREOF, the undersigned have set their hands hereto as of the 12th day of November, 2019.

/s/ James Schoeneck	/s/ Pat Cotroneo
James Schoeneck	Pat Cotroneo
Interim Chief Executive Officer	Senior Vice President, Finance and
	Chief Financial Officer

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of FibroGen, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

EXHIBIT T

BUYFRSSTRIKE!

Proof Denies Faith

ABOUT

BUYERSSTRIKE! BOOKSHELF

BUYERSSTRIKE! MAXIMS

INSTITUTIONAL MEMORY IR STAFFER HALL OF FAME

VICTORY LAP RE-UP: WHAT'S HARDER TO FIND, THE PYRENEES DATA SET IN AN FGEN PRESENTATION, OR ANDORRA ON A MAP? (FGEN, AZN)

[The following notes on Fibrogen (FGEN) are from November 2019. Re-upping it for a tiny victory lap. The company has known for years that the data was bogus. - Editor]

Both Fibrogen (FGEN) and AstraZeneca (AZN) have replied to reporters (but not the investing public at large) recently in response to the recent posts (see here and here) where we examined the Roxadustat DD-CKD data.

*ASTRA COMMENTS IN EMAILED STATEMENT ON ROXADUSTAT

• FGEN said in an emailed statement "We do not agree with this report, which contains many inaccuracies. The data presented at [American Society of Nephrology] reflect the analytical methods and study pools agreed upon with the FDA

Here at BuyersStrike! HQ we take accuracy seriously and if there is a material error of fact in a post, we will gladly set the record straight, and punish the offending intern with complicated coffee orders and only bags of nickels to pay the pizza guy. However, we believe that both Fibrogen's and AstraZeneca's responses do nothing more than continue to misdirect investors and fail to address the key points of the posts. So, here are some specific questions for both AZN

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and FGEN (and their sell side shills) to answer in order to truly clarify the safety data for Roxadustat.

Fibrogen:

In a Bloomberg article published on November 12, Fibrogen is reported to have replied to the author in an email statement that "[the report] contains many inaccuracies". Yet Fibrogen fails to point out a single one. Nobody here at HQ will be holding their breath waiting for FGEN to actually set the record straight. While they try to gin up even a single "inaccuracy", perhaps CEO Jim Schoeneck would also like to answer the following questions:

- Why do you present the ITT data for the NDD-CKD population but not for the DD-CKD population? This is a very simple analysis to perform and you already have the data. Appreciate that it is YOUR unwillingness to share it that causes smart investors to be skeptical.
- Why did you omit the PYRENEES study from the pooled statistical analysis when it compares Roxadustat to the prevailing standard of care? The weak excuse that two different active comparators were used in the PYRENEES study ignores the reality that:
 - Both were considered standard of care (which was the intention of the study).
 - There is an unquestionable death imbalance (more deaths in the Roxadustat arm).
- Astute readers will note that you refuse to state in any of your press releases that for the pooled analysis of ROCKIES, HIMALAYAS, PYRENEES, and SIERRAS:
 - There is no death imbalance in the ITT population.
 - The safety endpoint of non-inferiority in time to all-cause mortality in the intent-to-treat DD-CKD population was met.
 - The safety endpoint of non-inferiority in time to first MACE in the intent-to-treat DD-CKD population was met.

You have a fantastic opportunity to do so right now. Go ahead Jim.

■ In the November 11th conference call with investors and analysts, a simple yes/no question was asked but was not answered:

Answer - Xiaodong Zhang: So the noninferiority margin of 1.3 is already in agreement or not?

Answer – K. Peony Yu: So we are talking about the analysis plan, meaning how do you pool, what's the pooling strategy and the analysis plan, how to analyze the data. When you talk about NI margins, you're talking about the standard for assessment, right? And as I mentioned earlier, that we expect that all regulators will assess the data based on the very — all the — on the entire application of the NDA. And based on our dialogue with FDA over the past 6 years and the data, as we have shown, we are confident that we do have what it takes for this drug to be favorably evaluated.

As appears to be the case with analysts these days, the person asking the yes/no question seems completely fine with a confusing, non-binary (or is the proper terminology "reality-non-conforming") answer and doesn't bother to follow up. We believe this simple question should have been answered. This is another great opportunity for Schoeneck and his crew at Fibrogen to set the record straight and provide an answer to the question.

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Public companies do not generally hide good news. If Roxadustat is safe in the DD-CKD population FGEN should gleefully disclose the full data set so physicians and investors alike can evaluate it on its merits.

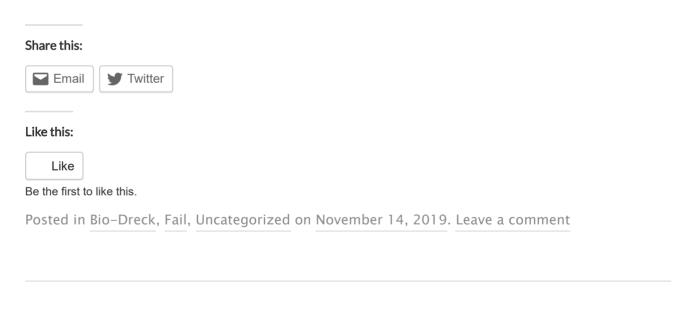
AstraZeneca (AZN):

AstraZeneca, also in an emailed correspondence to a Bloomberg reporter stated "the exclusion of the Pyrenees data from the safety analysis was agreed upon with the regulator." We understand that AstraZeneca may not have any input into the statements Fibrogen makes so in addition to the questions above, there is a very simple one below:

Why would the regulators agree to omit from the safety analysis a clinical study with a clear all-cause mortality imbalance that sheds light on the safety profile of a drug?

Ah, the sound of crickets in Andorra.

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← Climbing the Pyrenees (FGEN,AZN, 4053JP)

RE-UP: Everything Old is New Again: The Continuing Saga of Bioscam Nanoviricides (NNVC) →

EXHIBIT U

S&P Global
Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Tuesday, February 25, 2020 8:30 PM GMT

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Call Participants

EXECUTIVES

Enrique A. Conterno *CEO & Director*

ANALYSTS

Geoffrey Craig Porges *SVB Leerink LLC, Research Division*

Presentation

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Relatively recently appointed CEO, Enrique Conterno, and other members of the FibroGen team. Hi, Peony. So welcome to GHC this year.

Enrique A. Conterno

CEO & Director

Thank you, Geoff.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Your first GHC, how is it going?

Enrique A. Conterno

CEO & Director

I think it's going awesome. We had a packed agenda today, met with a number of investors. Very good.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division Good.

Question and Answer

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes. So let's jump right in. You mentioned a lot of questions about the launch in China. How's the launch in China going? Are you actually commercial at this point? Great news on the NRDL, but that was last year's news. So how are things going this year?

Enrique A. Conterno

CEO & Director

Well, the NRDL was an important achievement. It was last year's news, but it was effective as of January 1. We are very much tracking, I think, and we're very encouraged with what we're seeing when it comes to both hospital listings and demand on those hospital listings. Honestly, I'm pretty impressed with what the team has achieved.

Of course, we also have the coronavirus right now in China, which has meant that it is difficult to, if not impossible, to access any hospitals, and clearly, that has a bit of an impact.

Roxa has a bit of a unique position in China for a number of different reasons. But as an oral product, clearly, you really don't need to go to the hospital. So when it comes to, for example, PD patients and so forth, it represents an interesting alternative for patients that really don't want to go into the hospital at this point in time.

So far, I think we are very pleased with what we're seeing despite the fact that we have the coronavirus.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. And how is it actually working? I mean, I think your price was \$2,100 or something like that and obviously equivalent in local currency. And how much of a discount are you required to take once you get the local or provincial reimbursement? And then could you talk about, in the initial demand, how patients are -- do they have significant out-of-pocket burden? Can you kind of cover that out-of-pocket burden?

Enrique A. Conterno

CEO & Director

Sure. So I think what we've shared is that the net price that we estimate would be, getting for a patient for a full year in China, is about \$1,500. The out-of-pocket is going to be dependent on the different provinces and also whether it's a dialysis patient or an NDD patient. But I think it's -- we're still in the early stages. Keep in mind that provinces were given through Q1 to be able to implement the reimbursement system. But so far, I think we are pleased with the demand. But we have to -- it's very early, I think, in the stages of the launch for us to make too many assessments in terms of what is the exact out-of-pocket that patients are paying.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. And are you finding that you're getting more traction in the dialysis patients or the nondialysis patients? Very much a very different context.

Enrique A. Conterno

CEO & Director

Yes. It's difficult to say at this stage. But clearly, dialysis is a pretty big focus for us, given that those patients are treated for anemia. So -- and there is a pretty big opportunity. So that's really where the initial focus and the uptick that we expect initially is going to be, keeping in mind that the NDD opportunity also in China is a very significant one from a [patient's] perspective.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes, it's obviously large. Now one of the questions that keeps coming up is the question of the ownership of the Chinese joint venture. Could you talk about the option of spinning that out or capitalizing that independently? How -- who makes the decision on that? How you might come to a decision about that?

Enrique A. Conterno

CEO & Director

Yes. Clearly, as we think about China, there are many options the company have. At this point in time, I'm not commenting on our -- the options that we have for our Chinese business. I think my focus, and appropriately so right now as we're launching the product, have to be ensuring that we are getting the fundamentals right and that we can build and create a very significant ongoing business. I think I want to make sure that there is the focus on the task at hand right now.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. Now is there any intention, for example, to licensing complementary renal products or anything into that entity that you have there?

Enrique A. Conterno

CEO & Director

We're always open to think about those opportunities, but it's not a focus for us right now. I think our focus is, once again, to grow roxa to be the type of transformational medicine that it can be. It's a pretty unique opportunity to have this type of medicine, and China represents a very significant market. Keep in mind, it is the largest dialysis market in the world and we want to -- and we have achieved reimbursement across CKD anemia and a reasonable price. So we need to make sure that we capitalize in the hand that we have right now.

We're always open to look at additional opportunity, in particular, complementary opportunity, but I think it's fair to say that, that is not the focus today.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. Let's just pivot to talk about the U.S. market. Is your expectation that you will get essentially the same labeling and market opportunity in the U.S. as you've been given in China?

Enrique A. Conterno

CEO & Director

Yes. So clearly, in the U.S., we submitted our application at the end of last year. We've been -- our filing has been accepted, and we have a PDUFA date of December 20 of this year. We submitted for both, dialysis-dependent and nondialysis-dependent patients, patients with anemia. So we are planning to basically pursue both opportunities.

Just to give a sense of the magnitude of the opportunity. As you know, in the U.S., there's about 600,000 patients on dialysis. About 90% of those patients are treated for anemia. That gives you about 5,500 patients -- sorry...

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

550,000.

Enrique A. Conterno

CEO & Director

550,000 patients that, in terms of patients, that is the addressable opportunity with roxadustat.

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If we think about NDD, the opportunity -- the addressable opportunity is about 10x as large. We're looking at an opportunity of about 5 million addressable patients. Keep in mind that the number of patients treated in this segment is basically in the low double digits. So you -- we are thinking about...

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Sorry. As a percentage of that total treated for anemia?

Enrique A. Conterno

CEO & Director

Correct.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. That's what I thought you said.

Enrique A. Conterno

CEO & Director

So we are looking at basically an opportunity, yes, patients that are treated, but also, I think it's going to be important here, the significant expansion opportunity to be able to reach more patients for -- and for those patients to be treated.

Let's keep in mind that before EPO had some of the issues and they received a black box, the rate of treatment of anemia in this population was significantly higher, right?

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes. How high did it get? From recollection, it was in the high 20s, something like that?

Enrique A. Conterno

CEO & Director

That is correct. I think the figures that I've seen is, when you look at the prior 12 months of going into dialysis, up to 30% of those patients used to be treated. That number today is closer to 14%.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

And how many do you think are actually sufficiently anemic to qualify for the label that you expect to get?

Enrique A. Conterno

CEO & Director

Well, I think it's -- there are several questions there, a question on the label. But I do think that's the addressable population. So I'm giving you the number of the addressable population that we basically expect. It is not, to me, as much a matter of whether those patients need to be treated, but how do we ensure that we convey the right messages and the benefits of treating some of those patients.

And maybe we can speak a little bit about that because there are significant benefits. Of course, when we look at -- and just to recap, we basically, for our U.S. submission, when it comes to NDD, we have, based on our agreement with the FDA, we have 3 pivotal trials: ANDES, ALPS and OLYMPUS. They comprise over 4,000 patients. And across all the studies, we reached our primary efficacy endpoint of raising hemoglobin.

But I don't think the story ends there. I think it is interesting to see the effectiveness -- the efficacy of the product across a broad range of patients, all right, that today don't have as many options whether they

are hyper-responders, or in some cases, maybe don't tolerate well EPO, or in some cases, they need much higher EPO doses over time.

I think we have a product here with a very nice profile, and importantly, I think in NDD, we basically saw much less transfusions. So if I recall the numbers, it's 15% of transfusions for patients that were on placebo. We only saw about 5% for patients that were on roxadustat. To me, I think that is a significant benefit, a significant benefit to the patient, but also to the payer and to the system.

And then, of course, there is this question of, well, how does the cardiovascular safety look like. As you're aware, I've had a chance to conduct and be part of a number of cardiovascular studies in my previous role, and I believe that the data that we have on cardiovascular safety is very compelling. We have agreed with the agency on both the post studies. So what are the studies that are going to be included as part of the analysis as well as the methodology that we will be utilizing for this particular segment we basically intend to treat, a statistical plan methodology.

And when we look at the data, basically -- we basically show to be comparable to placebo. And importantly, when we look at the subcomponents of MACE, we had, of course, MI and stroke and death and...

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Unstable angina.

Enrique A. Conterno

CEO & Director

Hospitalization for heart failure and hospitalization for unstable angina. We -- when we look at all those, in each -- for each one of the subcomponents, that confidence interval actually encompassed one which makes our data extremely clean in -- from a -- from my perspective when it comes to cardiovascular safety.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Enrique, sorry, can I just interrupt a moment. But from your prior experience, I think the FDA has pretty much said that up above the confidence interval of 1.3. And are you below that 1.3 for the subcomponents of MACE or just for overall MACE?

Enrique A. Conterno

CEO & Director

Yes. Keep in mind that the guidance that the FDA has provided is strictly for diabetes medicines, and the guidance for diabetes medicines is a 1.3 upper bound. So that means to -- we want to make sure -- the FDA wants make sure that products can exclude more than 30% risk of MACE events -- increased risk of MACE events.

There is no such guidance for CKD anemia, which means that the FDA will have a -- this will become a product review issue when they look at the benefit/risk profile of the product.

Now in the case of the diabetes products, just to go back, the FDA looks at MACE, so the 3 components. They don't look at the subcomponents when it comes to the upper bound because the numbers are a lot slower. So the confidence intervals tend to be a lot wider.

Now in our trial, when we look at the pooled analysis of ANDES, ALPS and OLYMPUS, we do basically see hazard ratios, about one -- slightly higher than one, but the upper bound in each one of these cases, is below 1.3. I do want to make the point the 1.3 number is an arbitrary number, okay? It was arbitrary for diabetes, and it's just a number. So at the end, I think it's a question of looking at what are the options. Keep in mind that the option today for those patients in NDD is really the EPOs actually have a black box and actually had a demonstration of -- sorry, a further trial. When we look at the stroke data, actually

stroke itself have a confidence interval to the right of one, so -- which is a statistically significant finding for higher stroke. So I...

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

For EPO?

Enrique A. Conterno

CEO & Director

For the erythropoietin, yes. So I find that our data, for all those reasons, is highly compelling. There are not many options, and we have a trial that, in my view, basically, shows safety against what I think is a very high hurdle of placebo.

It will be different if maybe we were in this particular population using another comparator, but I do like, and this question also comes quite a bit, which is why did you choose a trial against placebo instead of a trial against EPO.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes. Comes up.

Enrique A. Conterno

CEO & Director

Clearly, both choices are available, but I like the decision that we have made at FibroGen. This decision, of course, was made way before my time, but I think it gives you the best chance for a completely clean label because you are comparing yourself relative to placebo. And then, I think if you look at the data on its face, I do not believe that the data warrants a black box.

Now there's a lot of context when we discuss a black box, and of course, there's a black box for EPO agents in the class. I get that, and the FDA takes many considerations. But I do think that it is a pretty high standard, and I'm very excited and delighted with the results that we got in -- out of cardiovascular safety.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. A lot of pieces there. But -- so your base case assumption is that you do get the broad label presumably, and that potentially you don't get a black box for any of these cardiovascular events?

Enrique A. Conterno

CEO & Director

Yes. I think of -- it is the base case is, yes, that we have a broad label. And I think the base case for me is also that we get a black box, but we have the optionality of an upside of not be able to get one, given the data that we have. But that is an upside, I think, to our current plans.

We can be extremely successful. This would be a transformational medicine, regardless. Given the opportunity that we have, as we talked about 0.5 million patients on the DD side and 5 million patients on the NDD side and how do we ensure that as many of those patients are appropriately treated, I think, is going to be key.

Clearly, we are already thinking about our commercial plans. I already started discussions in many different forums with our partner, AZ in the U.S. I'm delighted to be working with AstraZeneca and I think it's going to be key for us to have a very strong launch.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Sorry, I'm conscious of time. So there's a bunch of things I want to try and get to, Enrique. First, do you expect an Adcom or not?

Enrique A. Conterno

CEO & Director

I think it's difficult to say. As you know, one, when you receive an acceptance of the filing, it is a typical time when you can get notice that you're going to receive an Adcom. We have received no indication at this stage of an Adcom. It doesn't mean that this is not a possibility, it could happen. We are preparing for an Adcom regardless. I think that -- because once they tell you, you have, I think, 45 business days to...

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Subscribe.

Enrique A. Conterno

CEO & Director

Yes. So we've got to prepare ahead of time and we're doing so right now.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. Reimbursement under the ESRD, whatever it is, reimbursement. So when do you apply for the NTAP, I think it is?

Enrique A. Conterno

CEO & Director

TDAPA?

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

TDAPA, yes. When do you apply for that? And when will you get an indication if you don't have access to that?

Enrique A. Conterno

CEO & Director

So TDAPA is an add-on payment for products they're going to be setting into the dialysis centers. Otherwise, they would be in the bundle, right? It's a policy basically incentivize so that innovation can come in and can be utilized. We believe that roxa meets all the requirements and conditions for TDAPA. So I say that is our base case for us is to be given an add-on payment, which would be outside of this capitated payments that these organizations receive.

The process is, once you get approval, you have the opportunity to submit for TDAPA. And typically, that process takes somewhere within the next -- within 3 months, and you're able to basically be able to get the reimbursement or not. But we feel good about that we meet the conditions and I think this can be very helpful for us to be included.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

And TDAPA is to be realized how long, 2 years?

Enrique A. Conterno

CEO & Director

Yes. It will be -- it's a 2-year payment. And then I think the idea is that the product will be then included in the bundle of hemodialysis.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. And during those 2 years, let's just hypothetically say that it's, I don't know, I'll pick a number say, \$300 a month is the cost to CMS for roxa. So they would pay the dialysis centers an extra \$300 a month for every patient they put on to roxa. And would they leave the capitated rate the same regardless of the fact that they're paying for EPO?

Enrique A. Conterno

CEO & Director

It's -- you're asking lots of questions. You know this TDAPA has been evolving and there are new guidelines even as of late last year, November. We have to see how all this is going to play out, but if you read how this is supposed to be implemented, yes, it is an add-on payment to whatever capitated payment there is. It doesn't mean that they couldn't adjust the capitated payments, but the add-on payment will be based on the average selling price plus 0, so it's a net 0 average selling price and so 100% of the average selling price. And this will be the payment that would be provided for those organizations to be -- for patients that are -- based on the number of patients that are basically on roxadustat.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. So this is important. So what do you think the likelihood is that they lower the bundled rate? I mean I'm just of the impression that changing the bundled rate is a complicated process with a lot of inputs and everything. It would seem to me to be pretty hard to lower the bundled rate at the same time they give you access to TDAPA reimbursement.

Enrique A. Conterno

CEO & Director

Yes. It's difficult to say how things are going to play out. I don't think that's the intent. I think the intent is to provide truly an add-on payment. But it's difficult to predict how things are going to play out. Regardless, though, whether they lower the capitated payment or not, the -- how the add-on payment is calculated is pretty clear.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes. No, that's clear. The add-on is clear.

Enrique A. Conterno

CEO & Director

So -- but that's really something that we think about, and of course, is concerning to roxadustat, making sure that we can get an acceptable price and making sure that there are incentives in the system so that they can basically include valuable innovation as part of the overall dialysis system.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. Sorry I keep asking questions about this. But do we have examples where oral analogs of injectable medicines have been added via TDAPA?

Enrique A. Conterno

CEO & Director

I am not familiar with this. Clearly -- and I think you're asking this question for -- due to this language in TDAPA of the oral-only language.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes.

Enrique A. Conterno

CEO & Director

The way we think about this is that, in this particular case, the reason that roxa can meet the criteria is because we need to be thinking of anemia functionally, and as part of that, of course, there are injectable alternatives to treat anemia. So we do believe that we could be included in TDAPA. That's the assumption that we're making right now.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes. Okay. Terrific. So last couple of seconds. Why doesn't anyone care about pamrevlumab? You're doing 3 Phase III trials.

Enrique A. Conterno

CEO & Director

We're not only doing 3 Phase III trials, but I view this as -- this is another jewel, and we have 3 trials on indications that are of high unmet medical need. If we think about IPF, pulmonary fibrosis, the effect size that we saw in Phase II, I think, is very impressive, not just when it comes to looking at forced vital capacity, but more importantly also, looking at some of the markers that we had when it comes to disease progression. Individually, that indication is very important.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Yes.

Enrique A. Conterno

CEO & Director

But now we also have pancreatic cancer, another very significant indication. And we -- those 2 trials Phase III programs are ongoing, and we're now starting DMD this year. Collectively -- I think the message is that, collectively, those indications are massive opportunity for a company the size of FibroGen. So very excited. The key for us is to accelerate our enrollment time lines, and we are working to ensure that is the case and that we can reach patients as quickly as possible.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Great. Okay. We've reached the end of our allotted time. So thank you very much, Enrique. Really appreciate it. Glad to see you here.

Enrique A. Conterno

CEO & Director

Yes. Thank you. Thank you.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Thank you for joining us.

Enrique A. Conterno

CEO & Director Very good.

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EXHIBIT V

S&P GlobalMarket Intelligence

FibroGen, Inc. NasdaqGS:FGEN FQ4 2019 Earnings Call Transcripts

Monday, March 02, 2020 10:00 PM GMT

S&P Global Market Intelligence Estimates

	-FQ4 2019-			-FQ1 2020-	-FY 2019-			-FY 2020-
	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS
EPS Normalized	(0.55)	(1.12)	NM	(0.25)	(0.33)	(0.89)	NM	(0.66)
Revenue (mm)	40.32	7.97	▼ (80.23 %)	62.51	284.57	256.58	▼ (9.84 %)	324.97

Currency: USD

Consensus as of Feb-13-2020 9:01 AM GMT

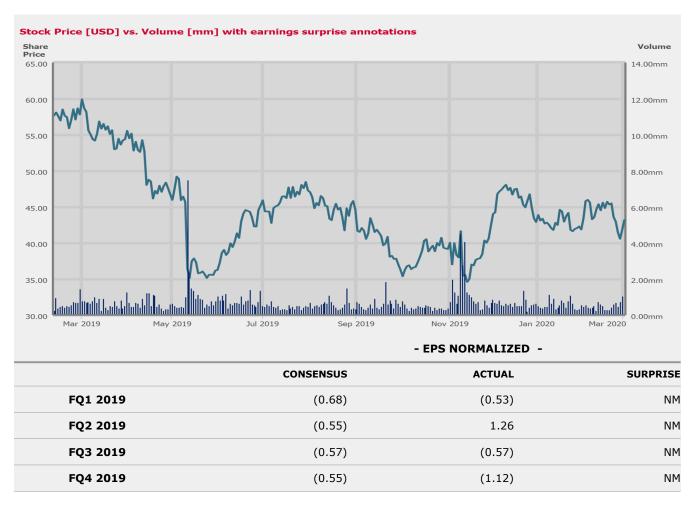


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Call Participants

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Presentation

Operator

Ladies and gentlemen, thank you for standing by. And welcome to the FibroGen Fourth Quarter and Full Year 2019 Conference Call. [Operator Instructions] Please be advised that today's conference is being recorded. [Operator Instructions]

I would now like to hand the conference over to your speaker today, Mike Tung. Thank you. Please go ahead, sir.

Michael Tung

Investor Relations Executive

Thank you, Justin. And good afternoon, everyone. Thank you for joining us on today's call to discuss FibroGen's performance for the fourth quarter and full year 2019. Today's call will be led by Enrique Conterno, our Chief Executive Officer; Enrique will be joined by Dr. Peony Yu, our Chief Medical Officer; Ms. Chris Chung, our Senior Vice President of China Operations, Dr. Elias Kouchakji, our Senior Vice President of Clinical Development, Drug Safety and Pharmacovigilance; and Mr. Pat Cotroneo, our Chief Financial Officer.

Before we begin, I would like to point out that we may make forward-looking statements regarding our business, including our collaborations with AstraZeneca and Astellas; financial guidance; the initiation, enrollment, design, conduct and results of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities; commercial results and results of operations; risks related to our business and certain other business matters. For risks and uncertainties regarding our business and statements made on the call today as well as factors beyond our control that may cause differences between current expectations and actual results, we refer you to our annual report on Form 10-K for the fiscal year ended December 31, 2019, all with the Securities and Exchange Commission. Copies of these filings can be found in the Investors section of our website. We undertake no obligation to update any forward-looking statement, whether as a result of new information, future development or otherwise.

The format for today's call includes prepared remarks from FibroGen's management team, and then we'll open the lines to take your questions. The press release reporting our financial results and business update and a webcast of today's conference call can be found on the Investors section of FibroGen's website at www.fibrogen.com. The webcast will be available for 30 days from today's date.

And now I'd like to hand the call over to Enrique Conterno, our CEO.

Enrique A. Conterno

CEO & Director

Thank you, Mike, and good afternoon, everyone. And welcome to our fourth quarter and full year 2019 earnings call. I'm excited to join the call today in my new role as FibroGen's CEO. I will start this morning by sharing a few thoughts about FibroGen and some initial impressions. I would also like to give you a sense of my initial areas of focus moving forward to deliver value to both patients and shareholders.

FibroGen has 2 world-class scientific platforms, and our success comes from keeping patients and science at the core of what we do. Before I provide an overview of our progress, I would like to take this opportunity to acknowledge Tom Neff, the founder of FibroGen, who passed away last year. I thank him for his invaluable contribution to making FibroGen what it is today, and I look forward to honoring his legacy.

I am highly appreciative of what the company has accomplished, and I look forward to continuing to build on this strong foundation. I have been spending time with my team, getting a clear sense of our strengths and challenges, and I've had the opportunity to hear from our shareholders and the broader investment community. My assessment is clear. FibroGen has a unique opportunity to leverage our world-class science in 3 areas of focus.

Number one, ensuring regulatory and commercial success of roxadustat, a transformational medicine in anemia therapy, first demonstrated in patients with chronic kidney disease, with great potential for expansion of treatment to other anemias.

Number two, accelerating the development of pamrevlumab in 3 high-value indications: idiopathic pulmonary fibrosis, locally advanced and resectable pancreatic cancer and Duchenne muscular dystrophy.

And number three, maximizing our scientific and medical understanding of HIF and CpG biology to provide future innovation.

Before we move into our review of 2019, I'd like to provide some overall perspective on the roxadustat commercial opportunity. As anemia associated with chronic kidney disease, or CKD, continues to grow in worldwide prevalence, our work has never been more important. Anemia is common in patients with CKD stages 3 to 5, and the rate of anemia increases as CKD progresses. We estimate that there are 4.9 million CKD non-dialysis patients with anemia in the United States. And that are up to 50% may be addressable based on our expected label. Additionally, there are approximately 0.5 million dialysis patients with anemia in the U.S.

In 2019, we made significant progress with roxadustat and achieved several critical advances, and we see continued momentum through 2020. Notably, the roxadustat NDA was submitted in the U.S. for the treatment of dialysis-dependent and non-dialysis-dependent CKD anemia late last year. And the filing was recently accepted with a PDUFA date of December 20, 2020.

In China, we and our partner, AstraZeneca, achieved roxadustat inclusion in the National Reimbursement Drug list, an important milestone to accelerate market adoption and coverage. Initial uptick of hospital listings and demand are encouraging.

In Japan, our partner, Astellas, received approval and launched roxadustat, which has the trade name, Evrenzo, in anemia in dialysis-dependent CKD patients, and submitted a supplemental NDA for the non-dialysis indication in this past January. Finally, in Europe, we and our partner, Astellas, look forward to the upcoming submission of roxadustat for treatment of dialysis and non-dialysis-dependent CKD anemia in the second quarter of this year.

Moving on to pamrevlumab, a first-in-class antibody, which inhibits the activity of connective tissue growth factor, a common factor in chronic fibrotic and proliferative disorders. In 2019, we initiated our ZEPHYRUS Phase III clinical program of pamrevlumab in patients with idiopathic pulmonary fibrosis. Last year, we also initiated our LAPIS Phase III clinical program of pamrevlumab for the treatment of patients with locally advanced unresectable pancreatic cancer. In Duchenne muscular dystrophy, we reported positive Phase II data in 2019, and we expect to begin the pivotal Phase III program in the second half of this year. All 3 of these indications are orphan diseases, with limited treatment options. Accelerating enrollment in all of these Phase III programs is a top priority for me in 2020.

We are in a position to create significant value for patients and shareholders. Our 2020 priorities are focused on getting roxadustat approved in the U.S., advancing pamrevlumab development and finally, leveraging our expertise in both hypoxia-inducible factor and connective tissue growth factor biology to expand our pipeline on novel drug candidates.

Now I'll turn it over to Peony, who will provide you with a more in-depth discussion of roxadustat.

K. Peony Yu

Chief Medical Officer

Thank you, Enrique, and good afternoon, everyone. 2019 was a great year for roxadustat, and I would like to review some of the highlights. The roxadustat NDA was submitted to the FDA for the treatment of anemia in both dialysis-dependent CKD and non-dialysis-dependent CKD patients in December 2019. And FDA has accepted our NDA filing with PDUFA date of December 20, 2020. Roxadustat was approved in China for the treatment of anemia in DD-CKD patients at the end of in 2018 and for the treatment of NDD-CKD anemia in August 2019. Chris will go into more detail later in the call when she provides an update on FibroGen China.

In Japan, roxadustat was approved for the treatment of anemia in DD-CKD patients in September 2019 and the supplemental NDA for NDD-CKD was submitted this past January. With positive momentum, we look forward to advancing roxadustat in 2020.

In the U.S., we continue to support the FDA's review of our NDA and expect approval before the end of the year. There has been no indication at this time the FDA will hold an advisory committee meeting, but we are preparing as if there were one.

To optimize our business success in the U.S., we and our partner, AstraZeneca, continue commercialization preparation to pave the way for roxadustat to become accessible to patients. With the robust efficacy and safety profile demonstrated in our large Phase III program of over 8,000 patients, we believe roxadustat can potentially better address CKD anemia than what is currently available to CKD patients on dialysis and those not on dialysis.

I shall first summarize key positive efficacy and cardiovascular safety results from the over 3,800 patient pool of dialysis-dependent patients, where roxadustat was compared to epoetin alfa, and patient had a average treatment duration of 1.8 years.

As reported at the ASM meeting, in dialysis patients, roxadustat met the primary efficacy endpoint with larger hemoglobin increase than epoetin alfa in each of the 3 pivotal studies and in the pool analysis, while mean achieved hemoglobin levels were within the intended range. Roxadustat-treated patients had lower transfusion risk than EPO patients, while lowering MACE+ risk in the dialysis patient pool. Notably, unlike ESA, roxadustat maintain efficacy without increasing dose requirements in the presence of inflammation. Importantly, less IV iron supplementation was required with roxa than with EPO.

Within the dialysis patient population, we are particularly excited about the cardiovascular safety results of the incident dialysis of population. These patients entered the study during the first 4 months of dialysis initiation and had an average treatment duration of 1.5 years. We enrolled over 1,500 incident dialysis patients in this program, the largest in this population ever conducted.

Here, we demonstrated a meaningful reduction in cardiovascular safety risk, as roxadustat-treated incident dialysis patients had a 30% lower MACE risk and a 34% lower MACE+ than epoetin alfa-treated patients. We believe the high-risk incident dialysis population is the right and most appropriate setting for comparison of roxadustat versus the epoetin alfa, since most patients are ESA-naive to prior to study entry.

Now moving on to our non-dialysis program. I will summarize key positive efficacy and cardiovascular safety results from the over 4,200 pool of non-dialysis-dependent patients, where roxadustat was compared to placebo. As a reminder, the vast majority of NDD patients in the U.S. receive no ESA treatment, especially after the ESA label change over the period of 2007 to 2011. And placebo control is the preferred standard for safety comparison.

In NDD patients, roxadustat was superior to placebo in the primary efficacy endpoint of mean change in hemoglobin level from baseline and significantly reduce transfusion risk compared to placebo. Because roxadustat is conducive to IR mobilization, we demonstrate the roxadustat's efficacy in patients with lower iron stores than required for ESA. 40% of the patients in our Phase III NDD studies have baseline iron stores below the minimum required for treating -- for treatment with ESA, and demonstrate the hemoglobin response to roxadustat was similar to that of patients with iron repletion.

With respect to cardiovascular safety, roxadustat was comparable to placebo in risk of MACE and MACE+, while achieved a mean hemoglobin level of 11 grams per deciliter. With this favorable efficacy and safety profile in addition to the convenience of oral dosing, we believe roxadustat can potentially overcome a number of hurdles of ESAs and expand anemia treatment in NDD patients.

Beyond CKD, we continued development of roxadustat for the treatment of anemia associated with myelodysplastic syndrome for chemotherapy-induced anemia, while evaluating for additional diseases. Our vision for roxadustat is to become the standard-of-care for anemias broadly.

Last December, we presented positive results from the open-label portion of the Phase III global study evaluating roxadustat for treatment of anemia in MDS patients at the Annual American Society of Hematology Meeting. In 2019, we also initiated a Phase II study in chemotherapy-induced anemia. CIA represents a large patient population whose anemia is often left untreated today.

To make roxadustat available to the rest of the world, our partner, AstraZeneca, in collaboration with our team, is submitting marketing application of roxadustat for CKD anemia in a number of countries. We've already submitted to Canada, Mexico and several Asian countries. It is great to see all this progress in the months, following the 3 permanent scientists, including Dr. Bill Kaelin, our long time adviser and collaborator, were awarded the 2019 Nobel Prize in Medicine for discoveries in oxygen sensing, which serve as the important scientific basis for the development of roxadustat. We appreciate the medical community's strong support for roxadustat and look forward to the opportunity in working with physicians, nurses and patients to improve anemia care globally.

I would now like to turn the call over to Chris Chung, who will discuss the recent developments in China.

Christine L. Chung

Senior Vice President of China Operations

Thank you, Peony. 2019 was also a milestone year for FibroGen China. Roxadustat was launched the middle of last year. This established FibroGen as a commercial stage company. Beyond FibroGen, it was a historical milestone in global drug development, in that, for the first time in history, China was the first-launch country for a first-in-class drug. Roxadustat was added to the 2019 National Reimbursement Drug List, or NRDL, effective January 1, 2020. Reimbursement by the government greatly reduces the copay portion for patients and is critical to market adoption.

As Peony already stated, in August, the NMPA approved roxadustat for non-dialysis. Roxadustat has the unique benefit of oral administration, and we believe the NDD approval will greatly extend the reach of roxadustat to patients-in-need beyond dialysis. FibroGen earned \$22 million in milestone payments from AstraZeneca, triggered by the NRDL inclusion.

Looking forward to 2020, with reimbursement for roxadustat now available on a national basis, our top priority is hospital listings. A drug needs to be listed in a hospital formulary before it can be dispensed for 90-plus percent of the potential market represented by government hospitals. This process is done on a hospital-by-hospital basis.

Given the transformative nature of roxadustat, an equally important priority for us is physician education. As for the market potential in China, we believe there are over 600,000 dialysis patients in China, making this the largest dialysis population in the world. It is expected to continue to grow in the foreseeable future at a low double-digit rate. We estimate the addressable population in non-dialysis with anemia to be around 2 million to 3 million patients.

Anemia treatment has historically been limited to oral iron, intravenous iron and ESAs. We believe the oral nature of roxadustat and the absence of a box warning could greatly expand the addressable NDD patient base as well as increased treatment rates and persistency in this population.

Coronavirus continues to be an evolving situation in China and beyond. While ensuring the health of our employees, our top priority is in making sure that roxadustat is available to patients. As of today, both our drug product facility in Beijing, and our API facility in Hangzhou, have returned to operations after a short period of shutdown. Our ability to conduct in person visits to physicians and hospitals continues to be affected, and we will continue to monitor and assess the situation closely.

I will now turn the call over to Elias Kouchakji, who will provide an update on the pamrevlumab program.

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Thank you, Chris, and good afternoon. I would like today to review our accomplishments with pamrevlumab over the last year and update you on our plan for 2020. In 2019, the FDA and the EMA,

both granted orphan drug designation for pamrevlumab and the treatment of the Duchenne muscular dystrophy, also known as DMD. This has strengthened our commitment to developing our novel antibody as a potential new treatment option for those suffering from this debilitating and progressive disease.

Also, in the last year, we began enrollment in our pivotal Phase III trials, in both idiopathic pulmonary fibrosis and in pancreatic cancer. These studies are ZEPHYRUS, a Phase III randomized, double-blind, placebo-controlled study; evaluating pamrevlumab and IPF; and LAPIS, a Phase III randomized, double-blind, placebo-controlled study in locally advanced unresectable pancreatic cancer.

In September of last year, Lancet Respiratory Medicine published our PRAISE Phase II study data in IPF. The published data for this randomized, double-blind, placebo-controlled study showed that both: one, the decline in forced vital capacity percent predicted; and two, the proportion of patient with the disease progression were significantly lower in the pamrevlumab group than in the placebo group.

In an accompanying editorial, Dr. Athol Wells of Royal Brompton Hospital wrote, "It is difficult to imagine a more encouraging Phase II trial." As we move forward with our Phase III program, we are gratified by the interest of our KOLs in the pulmonology community have shown in pamrevlumab as a potential new therapy for IPF.

In 2020, we are planning to accelerate and expand development of pamrevlumab. We are focused on accelerating enrollment of our ongoing ZEPHYRUS Phase III study and IPF. And to strengthen our regulatory submission, we now plan to add a second Phase III study. This change will mitigate the risk of having single study of approximately 560 patient, and now we plan to enroll approximately 340 patient in each of these 2 studies. The primary efficacy endpoint, and this is going to be the change from baseline and forced vital capacity, FVC. And the secondary endpoint will include clinical outcomes of disease progression, patient-reported outcomes and quantitative changes in lung fibrosis volume from baseline.

Moving on to the LAPC Phase III trial, LAPIS. We will continue to activate sites in the U.S. and globally to expand and accelerate enrollment of this approximately 260-patient trial.

In the second half of 2020, we also look forward to starting a Phase III trial evaluating pamrevlumab as a treatment for Duchenne muscular dystrophy. We are in discussion with the FDA and EMA to finalize the design of the program.

I will turn now the call over to our CFO, Pat Cotroneo, for the financial update. Pat?

Pat Cotroneo

Senior VP of Finance & CFO

Thank you, Elias. As announced today, total revenue for the quarter ended December 31, 2019, was \$8 million as compared to \$108.1 million for the fourth quarter of 2018. The current quarter revenue was made up of \$43.2 million in license and development revenue, plus \$1.1 million in net product revenue, less an adjustment relating to API pricing for Japan, which I will describe momentarily.

For the same period, operating costs and expenses were \$108.4 million, and net loss was \$98.1 million or \$1.12 per basic and diluted share as compared to operating costs and expenses of \$88.1 million and a net income of \$21 million or \$0.25 per basic share and \$0.23 per diluted share for the fourth quarter last year.

Included in our fourth quarter 2019 revenue recognition methodology is a total of \$22 million in milestones associated with the inclusion of roxadustat to the China NRDL in December. In the fourth quarter 2019, we recorded net product revenues of \$1.1 million for roxadustat sales in China. In addition, in the fourth quarter 2019, we recorded a reduction of \$36.3 million for commercial API delivered to Astellas in 2018, prior to approval and the establishment of the listed price in Japan. The original sale of API was based on an estimated listed price. The actual price was set by the Japanese Ministry of Health, Labor and Welfare in Q4 2019. Included in operating costs and expenses for the quarter ended December 31, 2019, was an aggregate noncash portion totaling \$22.1 million, of which \$17.4 million was a result of stock-based compensation expense as compared to aggregate noncash portion of \$15 million, of which \$13.7 million was a result of stock-based compensation expense for the same period in the prior year.

As stated in our Q2 2019 results, in accordance with U.S. GAAP, we recognized a total of \$180 million, comprised of \$50 million for an anticipated milestone from AstraZeneca related to the filing of the U.S. NDA, and \$130 million in anticipated milestones from Astellas in connection with the EU MAA filings, when such milestone achievement become probable. As noted earlier on this call, our NDA submission was accepted for review by the FDA in February, and we expect the Astellas MAA submission to occur in the second quarter of 2020. Based on these milestones and our latest forecast data, we estimate our 2020 ending cash to be in the range of \$720 million to \$730 million, assuming U.S. NDA approval in Q4 2020.

Looking ahead, we have a total of \$425 million in anticipated milestones expected over the next 18 months, which includes the \$180 million of milestones on NDA and MAA submissions already mentioned, plus \$245 million of milestones on approvals and first sale. The \$245 million is essentially equally split between our anticipated NDA and MAA approvals.

At December 31, 2019, FibroGen had \$627.1 million in cash, restricted time deposits, cash equivalents, investments and receivables.

Thank you. And I would now like to turn the call back over to Enrique.

Enrique A. Conterno

CEO & Director

In closing, this is an exciting time for FibroGen. Roxadustat is launching in China and Japan, and has been submitted in the U.S., Canada and other countries and soon in Europe. We are committed to bringing pamrevlumab as a first-in-class and best-in-class new medicines to patients in 3 high-value indications, namely idiopathic pulmonary fibrosis, locally advanced unresectable pancreatic cancer and Duchenne muscular dystrophy.

We look to re-energize our research agenda to deliver on our unique scientific expertise of both hypoxia inducible factor and connected tissue growth factor biology to create a fulsome pipeline of next-generation drug candidates.

We are in a strong financial position as roxadustat sales ramp up, with approximately \$630 million in cash and another \$425 million in anticipated roxadustat milestone payments expected over the next 18 months. In addition, we received partner reimbursement for development and commercialization of roxadustat in all geographies outside China. In China, we shared these expenses with AstraZeneca, 50-50.

I want to thank our team here at FibroGen for their dedication to improve the lives of patients that we serve. I would also like to thank Jim Schoeneck, who served as interim CEO and who will continue as Chairman of the Board.

Now I would like to turn the call back to the operator for questions. Justin?

Question and Answer

Operator

[Operator Instructions]

And our first question comes from Michael Yee from Jefferies.

Michael Jonathan Yee

Jefferies LLC, Research Division

Congrats, Enrique, on all the accomplishments recently. Two questions. One on pamrevlumab. I thought it was quite notable and you focused on accelerating IPF and pancreatic and just sort of the overall program. Maybe you could comment about specifically what you're doing to do that? Is that just site activation? Is that just more boots on the ground? Maybe talk about that. And whether you actually think you could get an interim on resection rate in pancreatic cancer in, say, 2021. Is that an achievable milestone?

And then on roxa, my question is, there is, obviously, some competitors around you, one of which will have Phase III data coming up shortly. Maybe you could comment on what we should keep in mind or what you're looking for and how to put that into context? I'm sure there'll be a lot of focus on that and compare it to your data.

Enrique A. Conterno

CEO & Director

Very good. Thank you, Michael. I'm going to ask Elias to address the question on pamrevlumab in terms of enrollment, what actions are we taking, Elias? And also, could we have an interim look on both LAPC as well as IPF? And I'm going to ask then Peony to address the roxa questions.

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Mike, thank you for your question. So first of all, as for the IPF study, we are accelerating the site activation in the U.S. -- not only in U.S., as globally. So we are actively very aggressively submitting all our CTAs and starting our European sites to be activated. Additionally, we are in more active contact with our sites, with our investigators. And we are more engaged with our community, the pulmonology community, and we are receiving a big interest. And a matter of fact, we are getting contacted, but some of these sites asking us about opening their sites for this study. So this is the first things we are doing at this time. And as you heard, this is going to be, again, the European studies. The second study is going to be activated.

Is the second part of your question is, can you remind me?

Michael Jonathan Yee

Jefferies LLC, Research Division

For pancreatic cancer, do you think you could get an interim on resection rate in 2021? Is that a very reasonable or achievable data point?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

So we are -- similarly, we are aggressively are going after the sites in the way of rolling sites. We all started to receive the CTA approval in Europe at the same time, and we are pushing us hard as possible to enroll these patients as fast as possible. And just a reminder, this patient is not prescreened because you have to wait for the patient to be diagnosed or unresectable, locally advanced and resectable before they get treated. If they are already treated, they cannot be in this study. So we are doing everything as possible that you're able to achieve these milestones, and we are pushing very hard to -- we expanded and increased the number of our sites at the same time.

Enrique A. Conterno

CEO & Director

Michael, maybe I can add. We're not providing, at this time, timelines when it comes to enrollment. We intend to provide more detailed timelines in the second half of this year for all of our trials when it comes to pamrevlumab. We are looking at the resection rate as one of the possibilities for us to request a meeting with the FDA for an accelerated approval. And we'll provide more details on that in the second half of this year.

Michael Jonathan Yee

Jefferies LLC, Research Division

Perfect. And then on roxa?

Enrique A. Conterno

CEO & Director

Peony?

K. Peony Yu

Chief Medical Officer

Okay. Mike, thanks for the question. We are aware that there are -- there's another HIF-PHI program that may be disclosing their Phase III data this year. To address your questions, I wanted to remind ourselves that roxadustat is the only HIF-PHI program that already demonstrated positive efficacy and safety data. So without seeing competitors' data is difficult to compare who has better data. And we know that in -- when you conduct a clinical trial, especially in safety outcome trial, one could expect a variety of outcome. And we are -- we have demonstrated a very favorable benefit and risk ratio. Now, however, I could comment on the Phase III study design, that we have designed a program to demonstrate safety in comparison to placebo and with the hope and confidence of gaining clean safety label for non-dialysis. And then in -- and we -- in incident dialysis, which is a highly relevant in treating anemia in dialysis patients, we have demonstrated a 30% reduction in MACE risk and a 34% reduction in MACE+ risk.

Based on what I have seen on trial -- Clinicaltrials.gov, none of the HIF-PHI Phase III program have the sample size even near what we have, which is over 1,500 patients.

Operator

And our next question comes from Geoffrey Porges from SVB Leerink.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Quickly, Chris, could you talk a little bit more about the launch of roxadustat in China, particularly how much of a delay do you think that the circumstances there are posing to you? And when do you think we might start to see a reduction ramp up and particularly, when you think you'll be through getting on to the hospital formulary list, at least the major institutions?

And then just a little bit more on R&D. Enrique, you mentioned sort of investing in both CTGF and HIF biology to broaden the pipeline. But could you give us a sense of what the opportunities you see there are because many companies in your situation would be saying, we need to go to another area, we have pretty good molecules already. So what you see is the opportunity from further investments around the biology of those targets from the pipeline?

Enrique A. Conterno

CEO & Director

Very good. Chris, take us on China now, then try to address the R&D question.

Christine L. Chung

Senior Vice President of China Operations

Absolutely. Geoff, so I believe your first question was about the impact of the coronavirus. So as we all know, it's an evolving situation. And as we know, for the last 30 to 45 days, many things were shut down in China. Many companies are returning to work. And as reported earlier, our 2 factories are back to full normal operations. We were extremely encouraged by the uptake in listings in the early part of the year immediately after NRDL inclusion and before the coronavirus outbreak. We believe as China returns to normal operations, the momentum will be regained. As to when that's happened, I think your guess is as good as anybody else's. We are generally optimistic that we have the team in place and with the strength of the AstraZeneca sales and key accounts team and the strength of the product, we think we could regain the momentum very quickly once that happens.

I believe the second question you had, Geoff, was when will the demand uptake be seen and how are we doing in terms of listings, in particular with the major hospitals. So in terms of demand, that comes, obviously, after only if you're listed. And we believe demand would come naturally after listing. As to how big of that demand is, again, it depends on the rate of the listings that we are focusing on in 2020.

In terms of the major hospitals, as most innovative companies will tell you, there are approximately 6,000 major academic centers in China. Roxadustat is no different in terms of when we expect to complete listings. I think if you look at historic data for all the multinationals, it takes anywhere from 5 to 6 years to list all the hospitals. However, historically, it's been the case that it took a while after launch to gain entry into NRDL. We were fortunate enough that, that time frame was not long for roxadustat. And we are optimistic that we could finish listings in a time frame shorter than what was historically the benchmark for multinationals.

Enrique A. Conterno

CEO & Director

Thank you, Chris. Clearly, one of the areas, Geoff, that I have been quite impressed when coming to FibroGen, and this has been a very positive surprise, has been to see the level of understanding that we have when it comes to both HIF biology and CTGF biology. It is known that both, in particular, HIF is involved in a number of different diseases. So the opportunities for us to explore and leverage this is quite unique.

And then when it comes to CTGF, similarly, the application for CTGF are likely in the fibrosis and cancer areas. Now when speaking about research, I think the aim here is very clear. It is to develop new drug candidates to be able to have a sustainable stream of innovation based on these 2 scientific platforms, where we are the leading edge of understanding and signed. So I'm very excited about that. And we, once again, will be providing more details on this with a caveat, of course, that we might not be able to share everything that we know for -- it may not be in FibroGen's best interest. But we intend to do so, provide more feedback on our research and our agenda in the second half of this year.

Operator

And our next question comes from Andy Hsieh from William Blair.

Tsan-Yu Hsieh

William Blair & Company L.L.C., Research Division

Congratulations on all the progress worldwide. So I want to ask a clarifying question about kind of the change in the IPF studies. So just wanted to really understand what caused the change from a 1 study, large IPF study to a 2 -- kind of 2 identical studies? Is that kind of prompted by the regulators or what? Just wanted to understand that dynamic.

Enrique A. Conterno

CEO & Director

Very good. Thank you for your question. I'm going to have Elias address the question earlier. Elias, the question relates to what caused the change in the IPF program to go from 1 study to 2 studies?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

So this was not triggered by any regulatory agency. This is triggered by our internal review and to take a look about the level of risk if it's going with a single study versus going with the 2 studies, that is most of the time is in the clinical development, the Phase III studies that you do 2 of them. And that will reduce the level of the statistical significance is required and this is any mishaps as this could be happening to reach that highly statistically significant. So when we assess that risk as we thought that there's a much better approaches to mitigate that risk. And at the same time, did not increase the size of the study tremendously. As you see, that is between the combined 2 studies versus 1 studies that the increase is manageable. That is the real reasons that for us as we move from 1 study into 2 studies.

We heard about this as a -- continuously previously about why we are doing single study. Is it riskier or not? And that is only as a step for a risk medication to ensure the success of the program.

Tsan-Yu Hsieh

William Blair & Company L.L.C., Research Division

Got it. And just a question on the potential Adcom. So just curious about the company's strategy. I know you guys have probably kind of preparing for that. Just the strategy or the plan of attack for the potential outcome, just given the fact that there's a lot of stakeholders, dialysis providers, CMS payers that might be watching very carefully at that, again, potential Adcom?

Enrique A. Conterno

CEO & Director

Very good. Yes, let me have Peony address the potential outcome for roxadustat. Peony?

K. Peonv Yu

Chief Medical Officer

Yes. So in our interaction with the FDA, there is no indication for an Adcom at this time. We will be -- we are preparing and will be well prepared if there is one. There are 3 possible time points that FDA may notify a sponsor of our Adcom, either before the NDA submission or at the time of initial -- 6 per 60 days of initial checklist before -- or by the time of the day 74 letter, where they inform the sponsor about NDA acceptance or any time during the FDA's review. And the final decision on Adcom or not really lies within the FDA.

Enrique A. Conterno

CEO & Director

Yes. And maybe just to add to Peony's response. Clearly, we are conducting a very thorough preparation regardless that we have not been given this indication or outcome. We have to prepare regardless. And in order to do that, we're following what is considered best practices for outcome preparation. Of course, we think about all stakeholders, but in particular, been able to address the questions that may come at the outcome. So that work is in progress.

Operator

And our next question comes from Joel Beatty from Citi.

Joel Lawrence Beatty

Citigroup Inc, Research Division

The first one is on the IPF Phase III program that switched from 1 trial to 2. Could you talk about how the powering of that Phase III program is affected from that switch? And do you anticipate that both Phase III trials will need to be successful? Or could the previous Phase II trial carry some weight as well?

Enrique A. Conterno

CEO & Director

Very good. Elias, the question is related to IPF and how is the powering effective, and whether both Phase III trials need to be successful. If you could address that.

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Yes. So we powered this study to plan for success. So that is our first aim. So we maintain a, the study to be highly powered similarly to the first study that we planned, which is we're not changing anything in that study than the size of the patient and enroll in that study. So we will maintain a very high level of powering of the study. And we -- based on our analysis of all the data that we currently have from our Phase IIa and Phase IIb studies. And we're taking in consideration is the available data and IPF from this other study that led to the approval of the other 2 product in perfenidone. So we combined all this data and that was the basis for our powering of our strategy. So I hope this has answered your question.

Joel Lawrence Beatty

Citigroup Inc, Research Division

Yes.

Enrique A. Conterno

CEO & Director

Yes. Thank you, Elias. Maybe I can also complement Elias' question. Joe, clearly, the change that we're making is to increase the likelihood of success for -- and yes, we are expecting both Phase III trials need to be successful. We need both trials to be successful for us to have a successful program.

Joel Lawrence Beatty

Citigroup Inc, Research Division

Understood. And then if I could ask one other question on roxadustat. Could you tell us about the launch preparations that are underway, particularly anything unique for the type of drug that it is, such as to TDAPA payment agreements or agreements with dialysis providers?

Enrique A. Conterno

CEO & Director

Yes. Let me try to address that question. Clearly, we are working on preparations for launch in the U.S. Really, we have a great partner in AstraZeneca that is leading that effort. And we will complement AstraZeneca when it comes to medical affairs and our science to ensure that we have a highly successful launch. Clearly, there are many aspects that one has to prepare for when it comes to U.S. launch.

And you're making comments about TDAPA. As you know, CMS, every year updates, what is called the end-stage renal disease prospective payment system, or commonly known as the bundle. This rule has continued to evolve and now has a policy that provides for this add-on payment, TDAPA, which basically provides a payment for drugs that otherwise would be included in the band. We clearly are looking when it comes to the dialysis segment at making sure that we're fully prepared and being -- it is always difficult to say how the rule will continue to evolve. But I, based on our discussion with the CMS, we believe that we're in a very good position. We also are looking to, of course, the non-dialysis-dependent segment. And as you know, we have, of course, patients that are covered through Medicare, in particular, Part D. And also patients on Medicaid and also patients on commercial insurance. So we are -- we need to make sure that at the end of the day, this product is going to be reimbursed broadly, and we are -- AstraZeneca is leading the charge to ensure that it is going to be the case.

Operator

And our next question comes from Paul Choi from Goldman Sachs.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

I want to ask with regards to the Phase III for roxa and MDS. There is a company facing a PDUFA hearing about to commercialize a drug for anemia of MDS and potentially in the not-too-distant future. So I was just wondering, as you think about the Phase III trial design, can you maybe just clarify for us, is

there an interim built-in where you do -- if you do see an adequate separation with regard to transfusion independence rates at interim? Is that something you could stop the early trial -- the trial early on? And then I had a follow-up.

Enrique A. Conterno

CEO & Director

Peony, could you address the question on MDS competition, and will we have an interim?

K. Peony Yu

Chief Medical Officer

Yes. Happy to. Thanks for the question, Paul. So we have paid 2 parts to our Phase III study in patients with MDS anemia. We have disclosed the first part, which is the open-label lead-in component and presented that positive result at ASH in 2019. The rest of the study is double-blind, placebo-controlled. And at this time, we do not have a plan for interim analysis. Now in terms of comment on the competition of the -- I believe that you must be referring to luspatercept, Paul, right?

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Yes. That's correct.

K. Peony Yu

Chief Medical Officer

Yes. It is a drug with a different mechanism of action. And that program is targeting only patients. MDS patients with ring deposits -- with ring sideroblast, RS positive, whereas our program does not have that restriction. And also, our agent is a HIF-PHI, and it is orally available. And while as the other drug is parenterally-administered. So they are -- those are some of the very obvious differences. And this is an area of a great unmet medical need, and we feel very comfortable wanting to, and could pursue this program and confident in the successful unit.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. And then just as a follow-up for pamrevlumab, specifically with regard to DMD. I know that you've disclosed which aspects of the program are advancing, but are you thinking maybe about a potential broader development program here and any other subpopulations? Any color there you could offer would be great.

Enrique A. Conterno

CEO & Director

So Elias, I think the question is here related to pamrevlumab in DMD. And if you could provide maybe some color on the broader program. Are we looking at other subpopulations as well?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

So currently, as you know, our study is in non-ambulatory, and we're concentrating this discussion, Paul, about the non-ambulatory. At the same time, during our discussion with the agencies, we are talking about the ambulatory population and looking at -- to see that how the program will look like is if we add this population to our side. We are in, as we said, in progressing the discussion with the agencies, including the AMA, not only the FDA, and we can give way more guidance on this in following earnings calls. But at this time, this -- the first study that we are concentrating on is the non-ambulatory study.

Operator

And our next question comes from Difei Yang from Mizuho Securities.

Difei Yang

Mizuho Securities USA LLC, Research Division

Just a couple. So with regards to the Adcom meeting, in the case if one was to take place, how much advance notice do you expect to get?

Enrique A. Conterno

CEO & Director

Peony, do you want to address the question on the Adcom, what is the advance notice?

K. Peony Yu

Chief Medical Officer

Difei, I believe FDA usually gives at least 45 business days before the actual meeting.

Difei Yang

Mizuho Securities USA LLC, Research Division

Okay. And the next one is that as you're getting closer to commercialization, how you see or what's your current thinking with regards to -- for the DD setting, that CMS setting, whether the drug will be in the bundle or not in the bundle?

Enrique A. Conterno

CEO & Director

Yes, it is difficult. I'm going to try to address that question. Clearly, it is difficult to predict whether we're going to be in the bundle or not, but we are preparing for both scenarios by having discussions with CMS. If we were to be in the bundle, as we have described, we believe that roxa would be eligible for TDAPA and the drug, the add-on payment, which would be key under that type scenario.

Operator

Thank you. And now I would like to turn the call back over to Enrique Conterno for closing remarks.

Enrique A. Conterno

CEO & Director

Thank you very much. We appreciate everyone's participation in today's investor call and your interest in FibroGen. Please follow-up with our Investor Relations team if you have any questions we have not addressed on the call, and enjoy the rest of your day. Thank you very much.

Operator

Thank you. And ladies and gentlemen, this concludes today's conference call. Thank you for participating, you may now disconnect.

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EXHIBIT W

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2019

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT **OF 1934**

> For the transition period from to. Commission file number: 001-36740

FIBROGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of incorporation or organization)

77-0357827 (I.R.S. Employer Identification No.)

409 Illinois Street San Francisco, CA

(Address of principal executive offices)

94158

(zip code)

Registrant's telephone number, including area code: (415) 978-1200

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, \$0.01 par value	FGEN	The Nasdaq Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes 🗷 No 🗆

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes \square No \square

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes 🗷 No 🗆

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act:

Large accelerated filer \square Accelerated filer Non-accelerated filer Smaller reporting company Emerging growth company П

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. \square

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes 🗆 No 🗷

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, computed by reference to the closing price as of the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2019, was approximately \$2,463.8 million. Shares of Common Stock held by each executive officer and director and stockholders known by the registrant to own 10% or more of the outstanding stock based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of common stock outstanding as of January 31, 2020 was 87,999,804.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K incorporate information by reference from the definitive proxy statement for the registrant's 2020 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than after 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report filed on Form 10-K and the information incorporated herein by reference, particularly in the sections captioned "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," contains forwardlooking statements, which involve substantial risks and uncertainties. In this Annual Report, all statements other than statements of historical or present facts contained in this Annual Report, including statements regarding our future financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "believe," "will," "may," "estimate," "continue," "anticipate," "contemplate," "intend," "target," "project," "should," "plan," "expect," "predict," "could," "potentially" or the negative of these terms or other similar terms or expressions that concern our expectations, strategy, plans or intentions. Forward-looking statements appear in a number of places throughout this Annual Report and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for roxadustat, pamrevlumab and our other product candidates, our intellectual property position, the potential safety, efficacy, reimbursement, convenience clinical and pharmaco-economic benefits of our product candidates, the potential markets for any of our product candidates, our ability to develop commercial functions, our ability to operate in China, expectations regarding clinical trial data, our results of operations, cash needs, spending of the proceeds from our initial public offering, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions described in the section of this Annual Report captioned "Risk Factors" and elsewhere in this Annual Report.

These risks are not exhaustive. Other sections of this Annual Report may include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. The forward-looking statements made in this Annual Report are based on circumstances as of the date on which the statements are made. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report or to conform these statements to actual results or to changes in our expectations.

This Annual Report also contains market data, research, industry forecasts and other similar information obtained from or based on industry reports and publications, including information concerning our industry, our business, and the potential markets for our product candidates, including data regarding the estimated size and patient populations of those and related markets, their projected growth rates and the incidence of certain medical conditions, as well as physician and patient practices within the related markets. Such data and information involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

You should read this Annual Report with the understanding that our actual future results, levels of activity, performance and achievements may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

PARTI

ITEM 1. BUSINESS

OVERVIEW

We are a leading biopharmaceutical company discovering, developing and commercializing a pipeline of first-in-class therapeutics. We apply our pioneering expertise in hypoxia-inducible factor ("HIF") and connective tissue growth factor ("CTGF") biology to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer.

Roxadustat, our most advanced product, is an inhibitor of HIF prolyl hydroxylase ("HIF-PH") that acts by stimulating the body's natural pathway of erythropoiesis, or red blood cell production.

In August 2019, roxadustat (China tradename: 爱瑞卓®) received marketing authorization in the People's Republic of China ("China") for the treatment of anemia caused by chronic kidney disease ("CKD") in non-dialysis-dependent patients. Roxadustat was approved in China for the treatment of anemia caused by CKD in dialysis-dependent patients in December 2018.

In September 2019, roxadustat (Evrenzo ®) was approved in Japan for the treatment of anemia associated with CKD in dialysis-dependent patients, and in January 2020, Astellas Pharma Inc. ("Astellas") submitted a supplemental New Drug Application ("NDA") in Japan for the treatment of anemia in non-dialysis CKD patients.

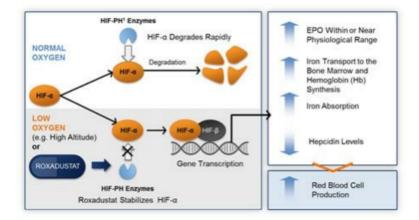
In conjunction with our collaboration partners, AstraZeneca AB ("AstraZeneca") and Astellas, we have completed the Phase 3 trials of roxadustat intended to support our NDA in the United States ("U.S.") and Marketing Authorization Application ("MAA") in the European Union and the United Kingdom ("Europe") for the treatment of anemia in CKD. Our NDA filing for roxadustat for the treatment of anemia in patients with dialysis-dependent CKD and in patients with non-dialysis-dependent CKD was accepted by the U.S. Food and Drug Administration ("FDA") in February, 2020. Astellas is in the process of preparing an MAA for submission to the European Medicines Agency ("EMA") in the second quarter of 2020 for the same indications. In addition, AstraZeneca has submitted applications for marketing approval of roxadustat in CKD anemia in Canada, Mexico, Taiwan, Philippines, and Singapore.

Beyond anemia in CKD, roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes ("MDS"). We also began a Phase 2 clinical trial of roxadustat in the U.S. in chemotherapy-induced anemia ("CIA") in the third quarter of 2019.

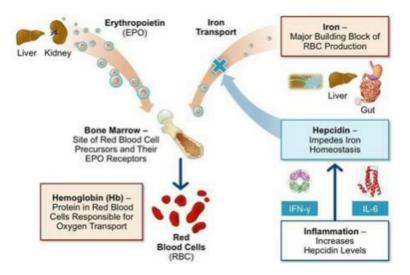
Pamrevlumab is our human monoclonal antibody that inhibits the activity of CTGF, a central mediator and critical common element in the progression of fibrotic and fibro-proliferative diseases. In 2019, we initiated a Phase 3 clinical program for the treatment of idiopathic pulmonary fibrosis ("IPF") and a Phase 3 clinical program for locally advanced unresectable pancreatic cancer. We also plan to initiate a Phase 3 program for the treatment of Duchenne muscular dystrophy ("DMD") in 2020.

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE

Roxadustat is an orally administered small molecule that treats anemia by a mechanism of action that is different from that of erythropoiesis stimulating agents ("ESAs"). Roxadustat, as a HIF-PH inhibitor, relies on the natural mechanism by which the body responds to low oxygen levels. HIF is a transcription factor comprised of a HIF-alpha and a HIF-beta subunit, both of which are required to stimulate erythropoiesis. Under normal oxygen conditions, the HIF-alpha subunit is targeted for rapid degradation through the activity of a family of HIF-PH enzymes. However, under low oxygen conditions, the HIF-PH enzymes cannot function and HIF-alpha accumulates. HIF-alpha then combines with HIF-beta, and the newly formed HIF complex initiates transcription of a number of genes involved in the erythropoietic process, which ultimately leads to increased oxygen delivery to tissues. Roxadustat works by reversibly inhibiting the HIF-PH enzymes, thus mimicking this coordinated natural erythropoietic response through genes encoding the proteins involved in iron absorption, mobilization and transport as well as stimulation of red blood cell progenitors.



The coordinated erythropoiesis activated by roxadustat includes both the stimulation of erythroid maturation, by increasing the body's production of erythropoietin ("EPO"), and an increase in iron availability for hemoglobin synthesis in part through a decrease in hepcidin levels, which is particularly important in patients with inflammation. Patients taking roxadustat typically have a transient increase in circulating endogenous EPO levels at peak concentration within or near the physiologic range naturally experienced by humans adapting to hypoxic conditions such as at high altitude, following blood donation, or impaired lung function, such as pulmonary edema.



By contrast, ESAs act only to stimulate erythroid maturation without a corresponding increase in iron availability, and are typically dosed at well above the natural physiologic range of EPO. The sudden demand for iron stimulated by ESA-induced erythropoiesis can lead to functional or absolute iron deficiency. We believe these high doses of ESAs are a main cause of the significant safety issues that have been attributed to this class of drugs. In addition, the lack of a coordinated increase in iron availability with ESAs may explain the hyporesponsiveness of patients with inflammation to this class of drugs. It also explains why patients taking ESAs need more IV iron supplementation and red blood cell transfusions than patients taking roxadustat do. Not only are IV iron and blood transfusions more costly than oral iron, but both are also associated with increased risk of hospitalization and death.

In contrast, the differentiated mechanism of action of roxadustat, which involves induction of the body's own natural pathways to achieve a more complete erythropoiesis, has the potential to provide a safer and more effective treatment of anemia, including in the presence of inflammation, which normally limits iron availability.

Background of Anemia in Chronic Kidney Disease

Chronic kidney disease is a progressive disease characterized by gradual loss of kidney function that may eventually lead to kidney failure or end-stage renal disease ("ESRD") requiring dialysis or a kidney transplant to survive. CKD affects 12% to 14% of the global adult population. CKD is more prevalent in developed countries, but is also growing rapidly in emerging markets such as China.

Anemia can be a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, a protein in red blood cells that carries oxygen to cells throughout the body. Anemia in CKD is associated with increased risk of hospitalization, cardiovascular complications and death, and frequently causes significant fatigue, cognitive dysfunction, and considerable reduction of quality of life.

Anemia is a complication of chronic kidney disease and becomes increasingly common as the disease advances. In the U.S., approximately 18 million adults have CKD Stages 3-5. Based on literature and market research, we estimate 25%, 50%, and 55% of CKD non-dialysis patients in Stages 3, 4, and 5, respectively, have anemia. This translates to an estimated 4.9 million CKD non-dialysis anemia patients, and we estimate that up to 50% may be addressable based on our expected label. Additionally, 90% of CKD patients on dialysis in the U.S., or approximately 0.5 million, have anemia.

When ESAs were introduced in 1989, they dramatically reduced the need for blood transfusions in CKD patients, which was a material development since transfusions reduce the patient's opportunity for a kidney transplant and increase the risk of infections and complications such as heart failure and allergic reactions. However, multiple randomized clinical trials with ESAs suggested safety risks of ESA therapies, and as a result, the anemia guidelines and approved labels have changed to more restrictive use of ESAs. In the U.S., while 93% of dialysis patients receive ESAs, in contrast, the percentage of patients who are on one or more ESAs at the time of dialysis initiation declined from 30% in 2006 to 13.6% in 2017, despite the well-recognized health risks of untreated anemia.

In addition to the safety concerns, which may be a greater impediment in the non-dialysis setting, other factors which contribute to the undertreatment of anemia in non-dialysis patients are related to the form of administration and accessibility of ESA products. ESAs are administered by infusion or subcutaneous injections, which is more difficult outside of dialysis centers or nephrology practices where non-dialysis patients are typically treated.

In the dialysis-dependent population, most patients start receiving ESAs when the patient is transitioning to dialysis care. Patients face significant increased risk of death, cardiovascular events and hospitalizations during the first year on dialysis, and concurrently initiating anemia therapy adds complexity and safety risks. In addition, patients at an advanced stage CKD are often affected by chronic inflammation that leads to functional iron deficiency, requiring IV iron, and reduced effectiveness of ESAs.

The Market Opportunity for Roxadustat

We believe there is a significant opportunity for roxadustat, a potentially safer and more effective anemia treatment, to address markets currently served by injectable ESAs. According to IQVIA MIDAS™ reports, global ESA sales in all indications totaled \$7.5 billion in 2018, driven primarily by \$5.4 billion sold in the U.S. and Europe, mostly for treatment of anemia in CKD. We further believe that the number of patients requiring anemia therapy will grow steadily as the global CKD population and access to dialysis care continue to expand, particularly in China and other emerging markets including the rest of Asia, Latin America, Eastern Europe, the Middle East, and the Commonwealth of Independent States. In addition, obesity, hypertension, and diabetes prevalence continue rising, and the mortality of ESRD patients is declining, particularly in many emerging markets.

Furthermore, we believe there is a significant opportunity for roxadustat to address patient segments that are currently not effectively served by ESAs, such as anemia in non-dialysis CKD due to under-diagnosis of CKD and under-treatment of anemia in this population. Awareness of health consequences and the burden of CKD may also improve the diagnosis rate of CKD, and thus anemia of CKD.

Recently Completed Roxadustat Phase 3 Clinical Program in CKD Anemia

The table below summarizes the basis of our roxadustat U.S. NDA and planned MAA filing in Europe. Our NDA filing was accepted by the FDA in February 2020 for CKD anemia in both dialysis and non-dialysis patients. The FDA has set a Prescription Drug User Fee Act goal date of December 20, 2020. We expect Astellas to submit the MAA in Europe in the second quarter of 2020.

Roxadustat Phase 3 CKD Anemia Clinical Program

		Number of Patients			
Study Sponsor, Number	Comparator	U.S.	Europe	China	Japan
NON-DIALYSIS					
FibroGen - FGCL-4592-060 (ANDES)	Placebo	92	22		
Astellas - 1517-CL-0608 (ALPS)	Placebo	59	97		
AstraZeneca - D5740C00001 (OLYMPUS)	Placebo	2,7	81		
Astellas - 1517-CL-0610	Darbepoetin alfa		616		
FibroGen - FGCL-4592-808	Placebo			151	
Astellas - 1517-CL-0310	Darbepoetin alfa				334
Astellas - 1517-CL-0314	None				99
Non-Dialysis-Dependent CKD Subtotal by Region		4,300	4,916	151	433
STABLE DIALYSIS		.,	.,,		
Astellas - 1517-CL-0613 (PYRENEES)	Epoetin alfa or Darbepoetin alfa		838		
FibroGen - FGCL-4592-806	Epoetin alfa			304	
Astellas - 1517-CL-0302	None				56
Astellas - 1517-CL-0307	Darbepoetin alfa				303
Astellas - 1517-CL-0308	None				75
Astellas - 1517-CL-0312	None				164
STABLE AND INCIDENT DIALYSIS					
AstraZeneca - D5740C00002 (ROCKIES)	Epoetin alfa	2,1	33		
FibroGen - FGCL-4592-064 (SIERRAS)	Epoetin alfa	74	11		
INCIDENT DIALYSIS					
FibroGen - FGCL-4592-063 (HIMALAYAS)	Epoetin alfa	1,043			
Dialysis-Dependent-CKD Subtotal by					'
Region		3,917	4,755	304	598
Total by Regulatory Approval Region		8,217	9,671	455	1,031
Combined Total to Support U.S. and Europe					
Approvals		9,6	571		

The primary efficacy endpoint was met in each of the pivotal studies for the U.S. NDA and Europe MAA, as shown below:

Summary of Results from Individual Phase 3 Studies of Roxadustat in CKD Anemia

Summary of Roxadustat U.S. and Europe Phase 3 Primary Efficacy Results

		Endpoint	-	Endpoint
Study Sponsor, Number	U.S. Primary Endpoint	Met	Europe Primary Endpoint	Met
NON-DIALYSIS				
FibroGen - FGCL-4592-060 (ANDES)	Superior to Placebo (p<0.0001)	✓	Superior to Placebo (p<0.0001)	✓
Astellas - 1517-CL-0608 (ALPS)	Superior to Placebo (p<0.001)	✓	Superior to Placebo (p<0.001)	✓
AstraZeneca - D5740C00001 (OLYMPUS)	Statistically-Significant Improvement in Hb Change Compared to Placebo	✓	Statistically-Significant Improvement in Hb Change Compared to Placebo	1
STABLE DIALYSIS				
Astellas - 1517-CL-0613 (PYRENEES)	Non-Inferior to ESAs	✓	Non-Inferior to ESAs	✓
STABLE AND INCIDENT				
DIALYSIS				
AstraZeneca - D5740C00002 (ROCKIES)	Statistically-Significant Larger Hb Increase Compared to Epoetin Alfa	✓	Statistically-Significant Larger Hb Increase Compared to Epoetin Alfa	1
FibroGen - FGCL-4592-064 (SIERRAS)	Superior to Epoetin Alfa (p<0.0001)	✓	Superior to Epoetin Alfa (p<0.0001)	✓
INCIDENT DIALYSIS				
FibroGen - FGCL-4592-063 (HIMALAYAS)	Superior to Epoetin Alfa (p=0.0005)	✓	Non-Inferior to Epoetin Alfa	✓

Pooled Efficacy Results in Non-Dialysis Patients

Superior at Raising Hemoglobin

Roxadustat superiority in efficacy was demonstrated in pooled efficacy analyses across the three Phase 3 dialysis-dependent studies and the three non-dialysis-dependent studies.

In the non-dialysis pool (4,277 patients from OLYMPUS, ANDES, and ALPS), the mean change in hemoglobin (from baseline to the average between Weeks 28-52) in roxadustat patients was also significantly larger than in placebo patients (1.85 g/dL vs. 0.13 g/dL, p<0.001).

Efficacy at Raising Hemoglobin Irrespective of Iron Replete Status

In the non-dialysis pool, roxadustat increased hemoglobin (by 1.94 g/dL) regardless of whether patients were iron-replete (patients shown to have sufficient baseline stores of iron in their body, TSAT \geq 20% and Ferritin \geq 100 ng/mL) or not iron-replete.

Reduction In Risk of Rescue Therapy and Transfusion

The risk of rescue therapy (blood or red blood cell transfusion, ESA use, or IV iron) was significantly lower in the roxadustat arm (8.9%) than the placebo arm (31.1%) in the pooled non-dialysis patients with a hazard ratio ("HR") = 0.19 (95% confidence interval "95% CI" of 0.16, 0.23), p<0.0001. The percentage of patients receiving red blood cell transfusions during the first year of treatment was also significantly lower in the roxadustat arm (5.2%) as compared to the placebo arm (15.4%) (HR (95% CI) = 0.26 (0.21, 0.32), p<0.0001).

Reduction of Decline in Kidney Function as Measured by eGFR

In a post hoc subgroup analysis of 2,438 non-dialysis patients with baseline eGFR≥15, the one-year decline in estimated glomerular filtration rate ("eGFR," a measure of the filtration function of kidney and renal disease progression) in roxadustat-treated patients (-2.8) was lower than that in placebo treated patients (-4.4), with a treatment difference of 1.6 mL/min/1.73m 2.

Reduction of LDL Cholesterol

In the pooled non-dialysis patients, roxadustat lowered low-density lipoproteins ("LDL"), with a mean change from baseline of -17.06 mg/dL compared to an increase of 1.30 mg/dL for placebo patients, a significant treatment difference of -19.83 mg/dL (p<0.0001).

Improvements in Quality of Life Measures

We have also observed improvements in quality of life. In the pooled analysis from the three non-dialysis studies, we observed statistically significant improvements from baseline to Week 12 in quality of life endpoints, including SF-36 Vitality subscale (p=0.0002), SF-36 Physical Functioning subscale (p=0.0369), FACT-AN Anemia subscale (p=0.0012), FACT-AN Total score (p=0.0056), and EQ-5D-SL VAS score (p=0.0005) when comparing roxadustat to placebo in CKD patients not on dialysis.

Pooled Efficacy Results in Dialysis Patients

Superior at Raising Hemoglobin

In the pooled dialysis studies (3,857 patients from HIMALAYAS, SIERRAS, and ROCKIES) the mean change in hemoglobin (from baseline to the average between Weeks 28-52) in roxadustat patients was significantly larger than in epoetin alfa patients (1.22 g/dL vs. 0.99 g/dL, p<0.001).

Efficacy at Raising Hemoglobin in Patients with Inflammation

In a subgroup of dialysis patients with inflammation (C-reactive protein ("CRP") levels over 4.9 mg/L), the mean change in hemoglobin (from baseline to the average between Weeks 28-52) was significantly higher in roxadustat-treated patients (1.29 g/dL) than epoetin alfa treated patients (0.96 g/dL, p<0.0001).

Lower Intravenous ("IV") Iron Requirements

In the dialysis pool, less mean monthly IV iron supplementation was required at Weeks 28-52 in patients receiving roxadustat versus patients receiving epoetin alfa in pooled analysis, p< 0.0001.

Reduction In Transfusion Risk

In the dialysis pool, during the first year of treatment, patients in the roxadustat arm had a lower transfusion risk (9.5%) as compared to the epoetin alfa arm (12.8%) (HR (95% CI) = 0.82 (0.679, 0.997), p=0.046).

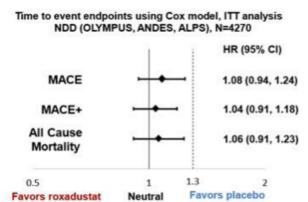
Pooled Cardiovascular Safety Results

In the U.S., the primary safety endpoint is time to first Major Adverse Cardiovascular Event ("MACE"), a composite endpoint of all-cause mortality, stroke and myocardial infarction. In Europe, the primary safety endpoint is the time to first MACE+ ("MACE+") which, in addition to the components in MACE, also includes hospitalization due to heart failure or unstable angina. However, the FDA in the U.S., and the EMA in Europe, will each review MACE, MACE+, and all-cause mortality separately, in addition to other endpoints.

The below cardiovascular safety analyses reflect the pooling strategy and analytical approach we agreed on with the FDA. Similar sets of analyses will be submitted to the EMA to serve as the basis for potential approval in dialysis and non-dialysis in Europe, and additional supportive analyses and sensitivity analyses as well as subgroup analyses were also included in the NDA and will be included in the MAA. However, the FDA and EMA will each conduct their own benefit-risk analysis and may use additional statistical analyses other than those agreed with the FDA or set forth below.

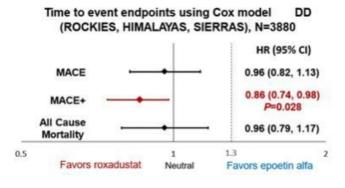
Non-Dialysis - Pooled Cardiovascular Safety Data

In our pre-NDA meeting, the FDA agreed that the intent-to-treat analyses followed for long-term safety results would be our primary cardiovascular safety analysis method for non-dialysis in the U.S. as it uses on-treatment and post treatment long term follow-up (until a common study end date) to account for the higher drop-out rate in the placebo arm. The figure below shows that in the 4,270 pooled non-dialysis patients (OLYMPUS, ANDES, and ALPS), the risk of MACE, MACE+, and all-cause mortality in roxadustat patients were comparable to that in placebo patients based on a reference non-inferiority margin of 1.3.



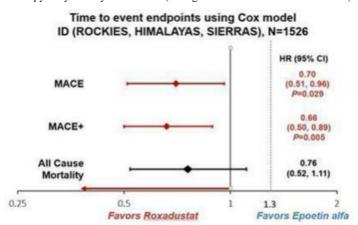
Dialysis - Pooled Cardiovascular Safety Data

In the pooled on-treatment analysis of 3,880 dialysis patients (HIMALAYAS, SIERRAS, and ROCKIES), the risk of MACE and all-cause mortality in roxadustat patients were not increased (based on a reference non-inferiority margin of 1.3), and roxadustat lowered the risk of MACE+ by 14% compared to the active comparator epoetin alfa, based on a hazard ratio of 0.86 and an upper bound of 95% CI under 1.0. The hazard ratios represent a point estimate of relative risk.



Incident Dialysis Subgroup - Pooled Cardiovascular Safety Data

In this program, incident dialysis patients are those who started participation in roxadustat Phase 3 studies within their first four months of dialysis initiation. In this clinically important subgroup of 1,526 incident dialysis patients, roxadustat reduced the risk of MACE by 30% and MACE+ by 34%, with a trend towards lower all-cause mortality. The lower MACE and MACE+ risks (compared to epoetin alfa) are based on hazard ratios of 0.70 and 0.66, respectively, with the upper bound of 95% CI under 1.0 in both. We believe this incident dialysis subpopulation is the appropriate setting for comparison of roxadustat versus epoetin alfa since most incident dialysis patients were ESA-naïve or have had only limited exposure to ESAs prior to study entry. In addition, the initiation of anemia therapy in this incident dialysis subgroup resembles clinical practice as the vast majority of US patients start anemia therapy early in dialysis treatment (during the first four months of treatment).



Non-Dialysis CKD Patients (ANDES) - FibroGen

ANDES is a 922-patient Phase 3, randomized, double-blinded, placebo-controlled trial designed to evaluate the efficacy and safety of roxadustat vs. placebo for the treatment of anemia in patients with later stage CKD (Stages 3, 4 or 5) who are not dialysis-dependent.

U.S. primary efficacy endpoint: roxadustat was superior to placebo in mean hemoglobin change from baseline to the average over Weeks 28 to 52 (2.00 vs. 0.16 g/dL, respectively, p<0.0001).

Europe primary efficacy endpoint: a higher proportion of roxadustat-treated patients (86.0%) achieved a hemoglobin response (defined as achieving a hemoglobin level of at least 11 g/dL on two consecutive visits during the first 24-weeks of treatment and a hemoglobin increase of at least 1.0 g/dL in subjects with baseline hemoglobin >8.0 g/dL, or an increase of at least 2.0 g/dL in subjects with baseline hemoglobin \leq 8.0 g/dL), as compared to placebo (6.6%), p<0.0001.

The proportion of subjects who received any rescue therapy (blood/red blood cell transfusion, ESA use, or IV iron) in the first 52 weeks of treatment was 8.9% in the roxadustat arm vs. 28.9% in the placebo arm (HR (95% CI) = 0.19 (0.138, 0.276), p<0.0001). The proportion of subjects who received blood/red blood cell transfusion in the first 52 weeks of treatment was 5.6% in the roxadustat arm vs. 15.4% in the placebo arm (HR (95% CI) = 0.26 (0.165, 0.406), p<0.0001).

The mean change in LDL cholesterol from baseline to average over Weeks 12-28 was -18.48 mg/dL (n=564) in the roxadustat arm vs. 0.22 mg/dL (n=269) in the placebo arm, with a treatment difference of -17.26 mg/dL (p<0.0001).

In this study, roxadustat-treated patients had a sustained reduction in hepcidin whereas placebo patients did not have a reduction in hepcidin. The mean change from baseline to Week 44 was $-22.1\mu g/L$ in the roxadustat arm vs. $3.88 \mu g/L$ in the placebo arm, for a treatment difference between the two arms of $-25.71 \mu g/L$ (95% CI: -38.523, -12.903).

In this study, subjects in the roxadustat arm had a substantially higher overall study drug exposure compared to subjects in the placebo arm. Study drug discontinuation was higher in the placebo arm compared to roxadustat arm, and the relative difference in discontinuation rates was especially pronounced in the lowest baseline eGFR category. The overall exposure-adjusted safety profile of roxadustat observed during this study was comparable with placebo and consistent with that expected in the CKD study population. The most commonly reported adverse events with roxadustat in this trial were nausea, hyperkalemia, constipation, and hypertension.

Non-Dialysis CKD Patients (ALPS) - Astellas

ALPS is Astellas' Phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of roxadustat for the treatment of anemia in CKD in 597 patients not on dialysis. The trial met its primary endpoints by demonstrating superiority in efficacy vs. placebo in terms of hemoglobin change from baseline at Weeks 28 to 52 (1.988 for roxadustat vs 0.406 for placebo, p<0.001).

Roxadustat was superior to placebo in its ability to lower LDL from baseline with an LS mean difference of -0.701 mmol/L (95% CI: -0.83, -0.57). Roxadustat was superior to placebo in delaying the need for rescue therapy (HR (95%CI) = 0.238 (0.17, 0.33), p<0.001).

The safety profile observed in this study was in line with the expected event profile in non-dialysis patients. Common adverse events in both treatment groups were ESRD, hypertension, peripheral edema, and decreased glomerular filtration rate.

Non-Dialysis CKD Patients (OLYMPUS) - AstraZeneca

OLYMPUS is AstraZeneca's Phase 3, randomized, double-blinded, placebo-controlled trial designed to evaluate the efficacy and safety of roxadustat vs. placebo for the treatment of patients with anemia in CKD Stages 3, 4 or 5 whose disease progression is moderate to severe and who are non-dialysis-dependent. The trial in 2,781 patients met its primary efficacy endpoint by demonstrating a statistically-significant improvement in mean change from baseline in hemoglobin levels averaged over Weeks 28 to 52 (1.75 g/dL) as compared with Placebo (0.40 g/dL).

Roxadustat also improved hemoglobin levels from baseline in a subgroup of patients with inflammation (CRP>5 mg/L), with a statistically significant mean increase of 1.75 g/dL, compared to 0.62g/dL with placebo.

Overall safety findings are generally consistent with the non-dialysis patient population. For all patients, the most commonly reported adverse events in the intent-to-treat analysis set were ESRD, pneumonia, urinary tract infection and hypertension.

Stable Dialysis CKD Patients (PYRENEES) - Astellas

PYRENEES is Astellas' Phase 3, randomized, active-controlled trial designed to assess the efficacy and safety of roxadustat vs. epoetin alfa or darbepoetin alfa, for the treatment of anemia in 838 patients with CKD who are dialysis-dependent. The trial met its primary efficacy endpoint: roxadustat was considered non-inferior to ESAs based on the mean change from baseline in average hemoglobin levels at Weeks 28 to 52 (0.397 vs 0.183; non-inferiority margin = -0.75).

Roxadustat was superior to ESAs in its ability to lower LDL from baseline with an LS mean difference of -0.377 mmol/L (95% CI: -0.451, -0.304). Roxadustat was superior to ESAs in reducing the need for monthly IV iron use (LS mean difference (95%CI) = -31.9 mg (-41.4, -22.4), p<0.001).

The safety profile observed in this study was in line with the expected event profile in dialysis patients. There was a greater proportion of deaths in the roxadustat treatment group compared with the ESA group; however, the study was not powered to assess risk of MACE events or death, as compared to the pooled analysis above. Common adverse events in both treatment groups were hypertension, arteriovenous fistula thrombosis, headache, and diarrhea.

Stable and Incident Dialysis CKD Patients (ROCKIES) - AstraZeneca

ROCKIES is AstraZeneca's Phase 3, randomized, open-label, active-controlled trial designed to assess the efficacy and safety of roxadustat vs. epoetin alfa, for the treatment of anemia in patients with CKD who are dialysis-dependent. The trial in 2,133 patients met its primary efficacy endpoint by demonstrating a statistically-significant improvement in mean change from baseline in hemoglobin levels averaged over Weeks 28 to 52 (0.77 g/dL) compared with epoetin alfa (0.68 g/dL).

Roxadustat also improved hemoglobin levels from baseline in a subgroup of patients with inflammation (CRP>5 mg/L, demonstrating a statistically significant improvement with a mean increase of 0.80 g/dL compared to 0.59 g/dL with epoetin alfa. Patients treated with roxadustat used less monthly IV iron (mean = 59mg) compared to those treated with epoetin alfa (mean = 91mg) from Week 36 to the end of the study.

Adverse events with roxadustat were generally similar to those seen in patients treated with epoetin alfa and commonly found in dialysis patients. In roxadustat-treated patients, the most commonly reported adverse events were diarrhea, hypertension, pneumonia, headache, and arteriovenous fistula thrombosis.

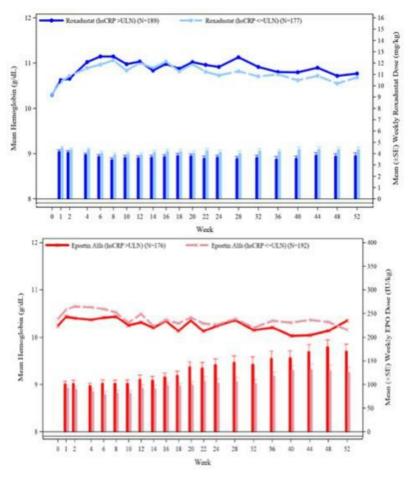
Stable and Incident Dialysis CKD Patients Study (SIERRAS) - FibroGen

SIERRAS is a 741-patient U.S. Phase 3, randomized, open-label, active-controlled trial to assess the efficacy and safety of roxadustat compared to epoetin alfa for the treatment of anemia in dialysis CKD patients who were receiving stable doses of ESA prior to study participation.

U.S. primary efficacy endpoint: the mean hemoglobin change from baseline to the average over Weeks 28 to 52 was 0.39 g/dL (roxadustat) vs. -0.09 g/dL (epoetin alfa), a least squares mean treatment difference of 0.48 g/dL (95% CI 0.37, 0.59). Roxadustat met the non-inferiority criteria as the lower bound of 95% CI was well above the non-inferiority margin of -0.75 g/dL. Roxadustat also achieved superiority, p<0.0001.

Europe primary efficacy endpoint: the mean hemoglobin change from baseline to the average over Weeks 28 to 36 was 0.54 g/dL (roxadustat) vs. -0.03 g/dL (epoetin alfa), a least squares mean treatment difference of 0.55 g/dL with a 95% CI (0.40, 0.69). Roxadustat met the non-inferiority criteria as the lower bound of the 95% CI was well above the non-inferiority margin of -0.75 g/dL. Roxadustat also achieved superiority over epoetin alfa, p<0.0001.

As seen in the figures below, in patients with inflammation (CRP>4.9 mg/L), roxadustat doses for maintaining hemoglobin levels were comparable to those with normal CRP and were stable over time as the effect on hemoglobin was durable, whereas epoetin alfa patients required higher mean doses in patients with inflammation (CRP>4.9 mg/L), doses which increased by approximately 50% from baseline after about one year. In these patients with inflammation (CRP>4.9 mg/L) mean change in hemoglobin from baseline to Week 18-24 was 0.61 g/dL in roxadustat vs. -0.03 g/dL in the epoetin alfa group, p<0.0001.



Subjects in the roxadustat group received lower mean IV iron during Weeks 28 to 52 than subjects in the epoetin alfa group (p=0.00091). Roxadustat-treated patients had a greater reduction in hepcidin as compared to ESA-treated patients. Additionally, a lower proportion of subjects on roxadustat received a red blood cell transfusion during treatment than the epoetin alfa group (12.5% and 21.1%, respectively, p=0.0337), with reduction in red blood cell transfusion risk by 33% compared with epoetin alfa; HR (95% CI) = 0.67 (0.466, 0.970), p=0.0337.

Mean LDL cholesterol levels decreased in the roxadustat group from baseline to the average over Weeks 12 to 28 (-13.70 mg/dL) but increased in the epoetin alfa group (1.23 mg/dL) with a treatment difference of -14.67 mg/dL (p<0.0001).

The incidence of treatment emergent adverse events was comparable in the roxadustat and epoetin alfa arms and were generally consistent with those typically expected in study patient population of ESRD on chronic dialysis therapy. The most commonly reported adverse events with roxadustat in this trial were nausea, hypertension, vomiting, and hyperkalemia.

Incident Dialysis CKD Patients Study (HIMALAYAS) - FibroGen

HIMALAYAS is a 1,043-patient Phase 3 randomized, open-label, active-controlled trial to assess the efficacy and safety of roxadustat compared to epoetin alfa, an ESA, for the treatment of anemia in CKD patients who have newly initiated dialysis treatment for ESRD and have had minimal or no exposure to an ESA prior to study participation.

U.S. primary efficacy endpoint: the mean hemoglobin change from baseline to the average over Weeks 28 to 52 was 2.57 g/dL (roxadustat) vs. 2.36 g/dL (epoetin alfa), a least squares mean difference of 0.18 g/dL, with the 95% CI of (0.08, 0.29). The non-inferiority criteria was met as the lower bound of the 95% CI was well above the non-inferiority margin of -0.75 g/dL, and superiority over epoetin alfa was also achieved, p=0.0005. In subgroup analyses, roxadustat was also superior to epoetin alfa in hemoglobin change from baseline regardless of iron repletion and inflammation status.

Europe primary efficacy endpoint: a higher proportion of roxadustat-treated patients (88.2%) achieved a hemoglobin response (defined as achieving a hemoglobin level of at least 11 g/dL on two consecutive visits during the first 24-weeks of treatment and a hemoglobin increase of at least 1.0 g/dL in subjects with baseline hemoglobin >8.0 g/dL, or an increase of at least 2.0 g/dL in subjects with baseline hemoglobin \leq 8.0 g/dL), as compared to an 84.4% responder rate in the epoetin alfa arm, with the lower bound of the 95% CI (-0.7%, 7.7%) of the treatment difference in responder rate well above the non-inferiority margin of -15%.

Roxadustat-treated patients had a statistically significant reduction in hepcidin, a key regulator of iron metabolism, as compared to ESA-treated patients. Roxadustat was shown to increase hemoglobin regardless of baseline inflammation status.

The most commonly reported adverse events with roxadustat in this trial were hypertension, diarrhea, and muscle spasms. The safety profile of roxadustat in this study was consistent with results from prior roxadustat studies.

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE IN CHINA

In August 2019, roxadustat (China tradename: 爱瑞卓®) received marketing authorization in China for the treatment of anemia caused by CKD in non-dialysis-dependent patients. Treatment for anemia caused by CKD in dialysis-dependent patients was approved in 2018.

In July 2019, results from our two China Phase 3 clinical trials were published in the New England Journal of Medicine.

In December 2019, roxadustat was included on the updated National Reimbursement Drug List ("NRDL") released by China's National Healthcare Security Administration. Roxadustat is included on the NRDL for the treatment of anemia in CKD.

Market Opportunity

The currently available forms of treatment in China for anemia in CKD include ESAs, oral iron, intravenous iron, traditional Chinese medicine, and combinations thereof. ESAs are the largest segment, which we estimate to be approximately \$275 million in sales, or approximately 80% of the total ESA market based on data from IQVIA China Hospital Pharmaceutical Audit. With the unique benefits of roxadustat to treat previously unaddressable patient populations, we believe the overall CKD anemia market will increase.

China is experiencing epidemiological changes in metabolic diseases due to economic development, urbanization and an aging population. Diabetes and hypertension are the leading causes of CKD in China, and rates have been growing over past two decades. We believe the increase in diabetes and hypertension prevalence will result in an increase of CKD anemia patients.

Dialysis-Dependent CKD

Based on the latest estimates and published data, we believe there are over 600,000 dialysis patients in China, making it the largest single-country dialysis population in the world. With the substantial growth rate of dialysis patients (over 10% per year from 2011 to 2017), the Ministry of Health and the Chinese Society of Nephrology have publicly recognized the need for further investment in dialysis infrastructure.

The prevalence rate of CKD dialysis patients that have anemia (defined as hemoglobin < 10g/dL) is estimated to be over 90%.

Dialysis treatment is delivered in the form of hemodialysis or peritoneal dialysis. In China, approximately 85% of dialysis patients with CKD are on hemodialysis. Hemodialysis is performed primarily in dialysis clinics within hospitals, most of which are publicly owned. This is in contrast to the U.S. where freestanding dialysis centers located outside of hospitals is common practice. With recent regulatory changes, the number of privately owned dialysis clinics is growing at a rapid pace, a trend that has provided additional capacity to meet the growing demand. The remaining 14-15% of CKD patients (approximately 100,000) are on peritoneal dialysis, which is self-administered at home by patients, a setting roxadustat, with its oral administration, is particularly well-suited for roxadustat. Peritoneal dialysis patients typically visit their nephrologists on a monthly basis at the hospital for monitoring and follow-up.

Non-Dialysis-Dependent CKD

We estimate that there are over 10 million Stage 3-5 non-dialysis CKD patients in China with anemia (defined as hemoglobin < 10g/dL). We believe the addressable population of non-dialysis patients with anemia (anemic patients that have been diagnosed and treated for CKD) is approximately 2-3 million, with 1-2 million in Stages 3 and 4 and 1 million in Stage 5 non-dialysis. This Stage 5 population that is dialysis-eligible but not receiving dialysis is characteristic of developing markets like China, and presents a particular opportunity for roxadustat, as many patients have severe anemia.

Unmet Medical Need and Roxadustat Differentiation in China

We believe there is a particularly significant unmet medical need for the treatment of anemia in CKD in China. Anemia is considered a risk multiplier for CKD patients and is commonly associated with increased rates of cardiovascular events, hospitalizations, CKD progression, and death. Several of the advantages that roxadustat, as an oral therapeutic, potentially offers over ESAs are particularly suited to address the unmet medical need in each of the three categories of CKD patients in China.

We believe there is chronic under-treatment of anemia within the CKD patient population on dialysis in China due in part to under-prescription of IV iron (often necessary for ESA treatment), and lack of efficacy in patients with inflammation. The most recent treatment guidelines published by the Chinese Society of Nephrology in 2018 recommended treatment to hemoglobin 11.0 g/dL to 12.0 g/dL. Even though over 70% of hemodialysis CKD patients, and approximately 60% of peritoneal dialysis CKD patients are treated with ESAs, based on the Chinese Renal Data System in 2015, less than 60% of dialysis patients reached 10.2 g/dL.

In the non-dialysis population and peritoneal dialysis population, only a small percentage of patients receive anemia treatment, and those who do, they receive only a minimal level of treatment, including patients who are eligible for dialysis and who have severe anemia. Roxadustat, as an oral medication, can be easily administered in any setting and stored at room temperature. Injectable drugs like ESAs present a challenge in China because even subcutaneous administration is performed at hospitals and not in the home, in part due to the difficulty in refrigeration and administration of injectable medicines. Frequent hospital visits, for the sole purpose of receiving injectable ESA treatment (as well as IV iron, which is often necessary with ESA treatment), can present a substantial logistical and financial burden to patients.

In the context of the rapidly growing China pharmaceutical market, we believe that the demand for anemia therapy will continue to grow as a result of an expanding CKD population, as well as the central government's mandate to make dialysis more available through government reimbursement and build-out of dialysis facilities. In addition, as the standard of living improves in China, the demand for access to innovative drugs increases. In this context, we believe that roxadustat is a particularly promising product for this market.

Commercialization

AstraZeneca is our commercialization partner for roxadustat in China. Under our collaboration agreement, AstraZeneca will lead commercialization activities and has responsibility for sales and marketing, and market access. FibroGen has responsibility for medical affairs, manufacturing (as the Marketing Authorization Holder), executing sales to distributors, and pharmacovigilance. FibroGen and AstraZeneca will work together to manage distribution.

Pricing and Reimbursement

In December 2019, roxadustat was included for the treatment of anemia in CKD on the updated NRDL released by China's National Healthcare Security Administration. The list is effective for a standard two-year period from January 1, 2020 to December 31, 2021. The negotiated price for a roxadustat 50 mg capsule is RMB 95. Roxadustat will be subject to price re-negotiation at the end of 2021.

We believe reimbursement is one of the two most critical market access factors for commercialization success in China, with the other being hospital listings. China is mostly a single-payor market with near universal healthcare provided by the government. Over 95% of the population receives healthcare coverage under one government-funded medical reimbursement plan or another, each with different levels of reimbursement. Commercial health insurance is available but is minimally adopted, and is seen as a supplement above and beyond government reimbursement.

Reimbursement for roxadustat will differ based on multiple factors including the CKD patient population (dialysis vs. non-dialysis), location, patient employment status, and if roxadustat is qualified into the "Critical Disease" or "Chronic Disease" insurance programs for such locations. We expect roxadustat reimbursement rates will be largely consistent with those ESAs listed on the NRDL. We believe in the next few years and in many parts of the country, dialysis patients will generally be reimbursed for 80-90% of their costs for roxadustat and non-dialysis patients in the 50-70% range.

Hospital Listing

Before roxadustat can be prescribed at a government hospital, which is 90% of the market in China, it has to be carried in the hospital formulary. The process of entry into the formulary is commonly referred to as "hospital listing". Decisions are made on a hospital-by-hospital basis, where hospital listing committees meet anywhere from every six months to every five years. Temporary listings can be used in the interim, where the head of the department could place an ad-hoc order with the formulary for a single or handful of patients for small quantities of roxadustat. These market access constraints impact all drugs, not just roxadustat. Consistent with the experience of other product launches in China, significant market uptake is usually seen a few years after launch, although in the case of roxadustat, it could be sooner given the inclusion in NRDL within 12 months of market approval.

Tendering

Tendering is a provincial level procedure. For drugs with multiple brands, it is a collective tender process for purchases by government hospitals of a medicine included in provincial or local medicine procurement catalogs. In the case of roxadustat, it is a more administrative process than for most drugs as roxadustat is currently the only drug of its class (HIF-PHI) available on the market. The tendering process of roxadustat is substantially complete in all 31 provinces in China.

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE IN JAPAN

In September 2019, roxadustat (Evrenzo®) was approved in Japan for the treatment of anemia associated with CKD in dialysis patients. Our collaboration partner Astellas launched Evrenzo in November 2019, targeting healthcare providers that care for approximately 330,000 dialysis patients across Japan.

In January 2020, Astellas submitted a supplemental NDA in Japan for the treatment of anemia in non-dialysis CKD patients, supported by three clinical studies in more than 500 Japanese non-dialysis patients with anemia associated with CKD.

ROXADUSTAT FOR THE TREATMENT OF CHEMOTHERAPY-INDUCED ANEMIA AND ANEMIA ASSOCIATED WITH MYELODYSPLASTIC SYNDROMES

Based on roxadustat's mechanism of action and safety and efficacy profile to date, we believe it has the potential to treat anemia associated with many other conditions, including CIA and MDS.

Background of Chemotherapy-Induced Anemia

As blood cell production in bone marrow is highly prolific, it is particularly vulnerable to the cytotoxic effects of chemotherapy used to treat cancer patients. Many chemotherapy agents directly impair hematopoiesis in bone marrow, including disruption of red blood cell production. The nephrotoxic effects of some cytotoxic agents, such as platinum-containing agents, can also result in decreased production of erythropoietin by the kidneys, further contributing to reduced red blood cell production. Radiation therapy has also been associated with hematologic toxicity.

Approximately 40% of total solid tumor cancer patients, or approximately 6.8 million people, undergo chemotherapy each year globally, including 1.7 million in the U.S. and 3.2 million in China. Eighty percent of those patients in developed countries and 40% of patients in China develop CIA. The incidence and severity of CIA depend on a variety of factors, including the tumor type or the level of toxicity of the therapy, and further increases with each successive chemotherapy round. We believe the addressable population is approximately 600,000 in the U.S. and 500,000 in China.

ESAs have been recommended for patients experiencing CIA with the desirable goals of improvement in anemia-related symptoms and the avoidance of blood transfusion which increases risk of infections and the risk of complications such as heart failure and allergic reactions. However, not all CIA patients respond to ESA therapy, which may be due to the etiology of their CIA or inflammatory comorbidity. ESA use also has associated toxicities, including increased thrombotic events, possible decreased survival and accelerated tumor progression, as published from randomized clinical trials and meta-analyses, that led to label restrictions and box warnings for ESAs in cancer populations in 2007, followed by the ESA Risk Evaluation and Mitigation Strategy ("REMS") program.

Market Opportunity for Roxadustat in Chemotherapy-Induced Anemia

ESA sales for CIA dropped significantly in the U.S. since the reported safety risks of ESA use in cancer patients in 2006, from estimated \$2.5 billion in 2006 to less than \$0.5 billion in 2019. During the same period, the prevalence of diagnosed CIA remained at similar levels, and is expected to grow slightly as a marginal decline of chemotherapy use is offset by an aging population.

We believe that if our clinical program shows an acceptable safety and efficacy profile, roxadustat would have the potential to address anemia in this population of patients undergoing chemotherapy, including, potentially, those patients with concomitant inflammation.

Clinical Development of Roxadustat in Chemotherapy-Induced Anemia

We began a Phase 2 proof of concept clinical trial of roxadustat in the U.S. in CIA in the third quarter of 2019. This is a single-arm open label study investigating the efficacy and safety of roxadustat for the treatment of anemia in patients receiving myelosuppressive chemotherapy treatment for non-myeloid malignancies, with treatment duration of 16 weeks, and will enroll up to 100 patients.

Background of Anemia in Myelodysplastic Syndromes

Myelodysplastic syndromes are a diverse group of bone marrow disorders characterized by ineffective production of healthy blood cells and premature destruction of blood cells in the bone marrow, leading to anemia. In most MDS patients, the cause of the disease is unknown.

Incidence and prevalence of MDS are not yet well understood, and may be greatly underestimated. MDS diagnosis became reportable under the World Health Organization oncology classification system only in 2001, and since then cases of MDS have been tracked by cancer registries.

The prevalence of MDS in the U.S. is estimated to be between 60,000 and 170,000, and continues to rise as more therapies become available and patients are living longer with MDS. We estimate that currently, approximately 70,000 patients are diagnosed with MDS in the United States.

Anemia is the most common clinical presentation in MDS, seen in approximately 80% of MDS patients, and producing symptoms, including fatigue, weakness, exercise intolerance, shortness of breath, dizziness, and cognitive impairment.

Limitations of the Current Standard of Care for Anemia in Myelodysplastic Syndromes

Stem cell transplant is the only potentially curative therapy for MDS, but it is not feasible in most patients due to their advanced age and frailty. The high rate of severe anemia leaves recurring red blood cell transfusions as the mainstay of care in MDS patients. Transfusion can result in direct organ damage through transfusional iron overload. Transfusion dependent MDS patients suffer higher rates of cardiac events, infections and transformation to acute leukemia, and a decreased overall survival rate when compared with non-transfused patients with MDS, and decreased survival compared to an age-matched elderly population. Patients receiving red blood cell transfusions may require an iron chelator in order to address toxic elements of iron overload such as lipid peroxidation and cell membrane, protein, DNA, and organ damage.

Lower-risk MDS patients represent approximately 77% of total diagnosed MDS population. Most national and international guidelines recommend use of ESAs for anemia only in lower-risk MDS patients presenting with symptomatic anemia with serum EPO levels at or below 500 mU/mL.

Even among the eligible subpopulation, the effectiveness of ESAs in treating anemia in MDS remains limited, with the best clinical study results showing 40% to 60% erythroid response rates, in studies where significantly high doses of ESAs were used, enrolled patients had low serum EPO levels, and in lower-risk categories. New strategies to broaden the eligible population, improve anemia and maintain adequate iron balance, as well as avoidance of transfusions, are highly desired in managing patients with MDS.

Market Opportunity for Roxadustat in Myelodysplastic Syndromes

We believe there is a significant need for a safer, more effective, and more convenient option to address anemia in patients with lower-risk MDS. Roxadustat, our orally administered small molecule HIF-PH inhibitor, stimulates the body's natural mechanism of red blood cell production and iron hemostasis based on cellular-level oxygen-sensing and iron-regulation mechanisms. Unlike ESAs which are limited to providing exogenous EPO, roxadustat activates a coordinated erythropoietic response in the body that includes the stimulation of red blood cell progenitors, an increase in the body's production of endogenous EPO, and an increase in iron availability for hemoglobin synthesis, which we believe is important in a broad range of MDS patients. Moreover, in anemia of CKD, roxadustat has demonstrated the ability in clinical trials to increase and maintain hemoglobin levels in the presence of inflammation as measured by CRP, where ESAs have shown limited effect. We believe that we may be able to replicate this result in MDS anemia patients, where it is not uncommon for patients to present with autoimmune and inflammatory conditions.

Clinical Development of Roxadustat in Myelodysplastic Syndromes

We are conducting a Phase 3 placebo controlled, double-blind clinical trial to evaluate the safety and efficacy of roxadustat for treatment of anemia in MDS in the U.S. and Europe. We continue to enroll this 160-patient randomized, double-blind, placebo-controlled Phase 3 clinical study of roxadustat in transfusion-dependent, lower-risk MDS patients, in which subjects are randomized 3:2 to receive roxadustat or placebo three-times-weekly. The primary endpoint is the proportion of patients who achieve transfusion independence by 28 weeks with secondary endpoints and safety evaluated at 52 weeks.

In the open-label dose-finding component of this study, 24 lower-risk, transfusion dependent MDS patients with anemia were enrolled in three sequential starting dose cohorts (1.5 mg/kg, 2.0 mg/kg, and 2.5 mg/kg), with roxadustat doses adjusted every eight weeks per a pre-defined algorithm based on hemoglobin response. Best supporting care including red blood cell transfusion was allowed, as needed, per investigator's discretion. Patients treated with roxadustat achieved a greater than or equal to 8-week transfusion independence rate of 38% in the first 28 weeks and 54% of patients had greater than or equal to 50% reduction in red blood cell transfusion over any eight weeks, from baseline. Roxadustat was generally well tolerated in each dose cohort. The dose level of 2.5 mg/kg was selected as the starting dose for the double-blind component of the study.

In China, we continue to enroll the open-label portion of our Phase 2/3 clinical trial to evaluate the safety and efficacy of roxadustat in non-transfusion dependent, lower-risk MDS patients with anemia. After the open-label portion we expect to begin the 135-patient double-blind, placebo-controlled Phase 3 portion of the study, in which subjects will be randomized 2:1 to receive roxadustat or placebo three-times weekly for 26 weeks. The primary endpoint for this study is percentage of patients achieving a hemoglobin response.

Research at FibroGen

The HIF-PH enzymes that are the targets of roxadustat belong to a broader family of enzymes known as 2-oxoglutarate (2OG)-dependent oxygenases. In humans, this family comprises more than 60 members that play important roles in a diverse range of biological processes including collagen biosynthesis, oxygen sensing, epigenetic regulation, nucleic acid modification/repair, and lipid metabolism. The first members of this enzyme family to be characterized were the collagen prolyl hydroxylases, which play a critical role in the biosynthesis of collagen and as a result, are potential targets for the treatment of fibrotic disease. The HIF-PH enzymes regulate the stability of the HIF transcription factor, which not only has therapeutic relevance for the treatment of anemia as exemplified by roxadustat, but also has implications for other diseases where activation of the HIF pathway would be expected to have beneficial effects. Other members of the 2OG-dependent oxygenase family with relevance to human disease include the Jumonji domain-containing histone demethylases, which are emerging cancer targets.

The fact that all members of the 20G-dependent oxygenase enzyme family use 20G as a co-substrate makes them viable targets for small molecule inhibitors that compete with 20G. FibroGen has been a world leader in inhibition of enzymes belonging to this family, and, our internal medicinal chemistry efforts have generated a large library of novel compounds designed to target the 20G-dependent oxygenase family.

PAMREVLUMAB FOR THE TREATMENT OF FIBROSIS AND CANCER

We were founded to discover and develop therapeutics for fibrosis and began studying CTGF shortly after its discovery. Our accumulated discovery research efforts indicate that CTGF is a critical common element in the progression of serious diseases associated with fibrosis.

From our library of human monoclonal antibodies that bind to different parts of the CTGF protein and block various aspects of CTGF biological activity, we selected pamrevlumab, for which we have exclusive worldwide rights. We believe that pamrevlumab blocks CTGF and inhibits its central role in causing diseases associated with fibrosis. Our data to date indicate that pamrevlumab is a promising and highly differentiated product candidate with broad potential to treat a number of fibrotic diseases and cancers.

We are currently conducting Phase 3 studies in pancreatic cancer and IPF and a Phase 2 trial in DMD. In the U.S., the FDA has granted Orphan Drug Designation to pamrevlumab for the treatment of IPF, locally advanced unresectable pancreatic cancer, and DMD. In addition, the EMA has granted Orphan Medicinal Product Designation to pamrevlumab for the treatment of DMD. Pamrevlumab has also received Fast Track designation from the FDA for the treatment of both IPF and locally advanced unresectable pancreatic cancer.

Overview of Fibrosis

Fibrosis is an aberrant response of the body to tissue injury that may be caused by trauma, inflammation, infection, cell injury, or cancer. The normal response to injury involves the activation of cells that produce collagen and other components of the extracellular matrix ("ECM") that are part of the healing process. This healing process helps to fill in tissue voids created by the injury or damage, segregate infections or cancer, and provide strength to the recovering tissue. Under normal circumstances, where the cause of the tissue injury is limited, the scarring process is self-limited and the scar resolves to approximate normal tissue architecture. However, in certain disease states, this process is prolonged and excessive and results in progressive tissue scarring, or fibrosis, which can cause organ dysfunction and failure as well as, in the case of certain cancers, promote cancer progression.

Excess CTGF levels are associated with fibrosis. CTGF increases the abundance of myofibroblasts, a cell type that drives wound healing, and stimulates them to deposit ECM proteins such as collagen at the site of tissue injury. In the case of normal healing of a limited tissue injury, myofibroblasts eventually die by programmed cell death, or apoptosis, and the fibrous scarring process recedes.

Multiple biological agents and pathways have been implicated in the fibrotic process, many of which converge on CTGF, a central mediator of fibrosis. In the case of cancer, the sustained tumor-associated fibrotic tissue promotes tumor cell survival and metastasis. CTGF is a secreted glycoprotein produced by fibroblasts, endothelium, mesangial cells and other cell types, including cancers, and is induced by a variety of regulatory modulators, including TGF-\(\text{B}\) and VEGF. CTGF expression has been demonstrated to be up-regulated in fibrotic tissues. Thus, we believe that targeting CTGF to block or inhibit its activity could mitigate, stop or reverse tissue fibrosis. In addition, since CTGF is implicated in nearly all forms of fibrosis, we believe pamrevlumab has the potential to provide clinical benefit in a wide range of clinical indications that are characterized by fibrosis.

Until recently, it was believed that fibrosis was an irreversible process. It is now generally understood that the process is dynamic and potentially amenable to reversal. Based on studies in animal models of fibrosis of the liver, kidney, muscle and cardiovascular system, it has been shown that fibrosis can be reversed. It has also been demonstrated in humans that fibrosis caused by hepatitis virus can be reversed (Chang et al. Hepatology (2010)). Additionally, we have generated data in human and animal studies that lung fibrosis progression can be slowed, arrested, or possibly reversed in some instances upon treatment with pamrevlumab.

Clinical Development of Pamrevlumab - Overview

We have performed clinical trials of pamrevlumab in IPF, pancreatic cancer, liver fibrosis and diabetic kidney disease. In eleven Phase 1 and Phase 2 clinical studies involving pamrevlumab to date, including more than 600 patients who were treated with pamrevlumab (about half of patients dosed for more than six months), pamrevlumab has been well-tolerated across the range of doses studied, and there have been no dose-limiting toxicities seen thus far.

Idiopathic Pulmonary Fibrosis

Understanding IPF and Current Therapies

IPF is a form of progressive pulmonary fibrosis, or abnormal scarring, which destroys the structure and function of the lungs. As tissue scarring progresses in the lungs, transfer of oxygen into the bloodstream is increasingly impaired. Average life expectancy at the time of confirmed diagnosis of IPF is estimated to be between three to five years, with approximately two-thirds of patients dying within five years of diagnosis. Thus, the survival rates are comparable to some of the most deadly cancers. The cause of IPF is unknown but is believed to be related to unregulated cycles of injury, inflammation and fibrosis.

Patients with IPF experience debilitating symptoms, including shortness of breath and difficulty performing routine functions, such as walking and talking. Other symptoms include chronic dry, hacking cough, fatigue, weakness, discomfort in the chest, loss of appetite, and weight loss. Over the last decade, refinements in diagnosis criteria and enhancements in high-resolution computed tomography imaging technology ("quantitative HRCT") have enabled more reliable diagnosis of IPF without the need for a lung biopsy.

The U.S. prevalence and incidence of IPF are estimated to be 44,000 to 135,000 cases, and 21,000 new cases per year, respectively, based on Raghu et al. (Am J Respir Crit Care Med (2006)) and on data from the United Nations Population Division. We believe that with the availability of technology to enable more accurate diagnoses, the number of individuals diagnosed per year with IPF will continue to increase.

There are currently two therapies approved to treat IPF in Europe and the U.S., pirfenidone and nintedanib. The approvals and subsequent launches of pirfenidone and nintedanib have clearly shown the commercial potential in IPF. Hoffmann-La Roche ("Roche") reported worldwide sales of approximately \$1 billion for 2018 and \$1.15 billion for 2019 for Esbriet® (pirfenidone). Similarly, Boehringer Ingelheim Pharma GmbH & Co. KG ("Boehringer Ingelheim") reported total sales of approximately \$1 billion for Ofev® (nintedanib) in 2017, and approximately \$1.2 billion in 2018.

Phase 3 Clinical Development - Randomized, Double-Blind, Placebo-Controlled Trials of Pamrevlumab in IPF

We continue to enroll ZEPHYRUS, our double-blind, placebo-controlled Phase 3 trial of pamrevlumab in IPF patients. In 2020, we will initiate a second IPF study similar in design to ZEPHYRUS. Each study will target approximately 340 patients. The primary U.S. efficacy endpoint for each study is change from baseline in forced vital capacity ("FVC"). The primary efficacy endpoint in Europe for each study is disease progression (defined by a decline in FVC percent predicted of greater than or equal to 10% or death). Secondary endpoints will include clinical outcomes of disease progression, patient reported outcomes, and quantitative changes in lung fibrosis volume from baseline.

PRAISE - Study 067 - Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial of Pamrevlumab in IPF

In September 2019, positive results from PRAISE, our randomized, double-blind, placebo-controlled Phase 2 clinical trial (Study 067), were published in *The Lancet Respiratory Medicine*. PRAISE was designed to evaluate the safety and efficacy of pamrevlumab in patients with mild-to-moderate IPF (baseline FVC percentage predicted of 55%), as well as topline results from two sub-studies that were added to evaluate the safety of combining pamrevlumab with approved IPF therapies.

In the double-blind, placebo-controlled 48-week portion of this study, 103 patients were randomized (1:1) to receive either 30mg/kg of pamrevlumab or placebo intravenously every three weeks. Lung function assessments were conducted at baseline and at Weeks 12, 24, 36 and 48. Quantitative HRCT assessments were performed at baseline and on Weeks 24 and 48.

Pamrevlumab met the primary efficacy endpoint of change of FVC percent predicted, a measure of a patient's lung volume as a percentage of what would be expected for such patient's age, race, sex and height. The average decline (least squares mean) in FVC percent predicted from baseline to Week 48 was 2.85 in the pamrevlumab arm (n=50) as compared to an average decline of 7.17 in the placebo arm (n=51), a statistically significant difference of 4.33 (p=0.0331, using a linear slope analysis in intent-to-treat population).

Pamrevlumab-treated patients had an average decrease (least squares mean) in FVC of 129 ml at Week 48 compared to an average decrease of 308 ml in patients receiving placebo, a statistically significant difference of 178 ml (p=0.0249, using a linear slope analysis in the intent-to-treat population). This represents a 57.9% relative difference. In addition, the pamrevlumab-treated arm had a lower proportion of patients (10%) who experienced disease progression (defined by a decline in FVC percent predicted of greater than or equal to 10% or death), than did the placebo arm (31.4%) at Week 48 (p=0.0103). The percentage of pamrevlumab patients who experienced disease progression and discontinued therapy was less than 15% of that in the placebo arm.

In this study, we measured change in quantitative lung fibrosis from baseline to Week 24 and Week 48 using quantitative HRCT. The pamrevlumab arm achieved a statistically significant reduction in the rate of progression of lung fibrosis compared to placebo using HRCT to measure quantitative lung fibrosis ("QLF"). The change in QLF volume from baseline to Week 24 for pamrevlumab-treated patients was 24.8 ml vs. 86.4 ml for placebo, with a treatment difference of -61.6 ml, p=0.009. The change in QLF volume from baseline to 48 weeks was 75.4 ml in pamrevlumab-treated patients vs. 151.5 ml in patients on placebo, with a treatment difference of -76.2 ml, p=0.038.

As in our previous open label Phase 2 study, a correlation between FVC percent predicted and quantitative lung fibrosis was confirmed at both Week 24 and 48 in this study.

We are not aware of any other IPF therapies that have shown a statistically significant effect on lung fibrosis as measured by quantitative HRCT analysis.

The treatment effects of pamrevlumab were demonstrated not only on change in FVC, a measure of pulmonary function and IPF disease progression, and change in fibrosis using quantitative HRCT, but pamrevlumab-treated patients also showed a trend of clinically meaningful improvement in a measure of health-related quality of life using the St. George's Respiratory Questionnaire (SGRQ) vs. a reduction in quality of life seen in placebo patients over the 48 weeks of treatment. The SGRQ quality of life measurement has been validated in chronic obstructive pulmonary disease. In the patients that were evaluated by the UCSD Shortness of Breath Questionnaire, pamrevlumab-treated patients had a significant attenuation of their worsening dyspnea in comparison to placebo.

Pamrevlumab was well-tolerated in the placebo-controlled study. The treatment-emergent adverse events were comparable between the pamrevlumab and placebo arms and the adverse events in the pamrevlumab arm were consistent with the known safety profile of pamrevlumab. In this study, as compared with the placebo group, fewer pamrevlumab patients were hospitalized, following an IPF-related or respiratory treatment-emergent adverse event, or died for any reason.

The double-blind, active-controlled combination sub-studies were designed to assess the safety of combining pamrevlumab with standard of care medication in IPF patients. Study subjects were on stable doses of pirfenidone or nintedanib for at least three months and were randomized 2:1 to receive 30 mg/kg of pamrevlumab or placebo every three weeks for 24 weeks. Thirty-six patients were enrolled in the pirfenidone sub-study and 21 patients were enrolled in the nintedanib sub-study. Pamrevlumab appeared to be well-tolerated when given in combination with either pirfenidone or nintedanib.

Study 049 - Open-Label Phase 2 Trial of Pamrevlumab in IPF

We completed an open-label extension of Study 049, a Phase 2 open-label, dose-escalation study to evaluate the safety, tolerability, and efficacy of pamrevlumab in 89 patients with IPF. During the initial one-year treatment period, pamrevlumab was administered at a dose of 15 mg/kg in Cohort 1 (53 patients) and 30 mg/kg in Cohort 2 (36 patients) by IV infusion every three weeks for 45 weeks. After 45 weeks of dosing, subjects whose FVC declined less than predicted were allowed to continue dosing in an extension study until they had disease progression. Nineteen patients from Cohort 1 (35.8%) and 18 patients from Cohort 2 (50.0%) entered the extension study. Efficacy endpoints were pulmonary function assessments, extent of pulmonary fibrosis as measured by quantitative imaging and measures of health-related quality of life. We presented data from our open-label Phase 2 IPF extension study (049) at the International Colloquium on Lung and Airway Fibrosis in November 2016, reporting that no safety issues were observed during prolonged treatment with pamrevlumab. Some of the 37 patients who enrolled in the extension study were treated with pamrevlumab for up to five years. Trends regarding improved or stable pulmonary function and stable fibrosis observed during the initial one-year study were also observed in the extension study.

In Cohort 1, we enrolled patients with a wide range of disease severity to assess safety and efficacy. Baseline FVC percent predicted for Cohort 1 was 43% to 90%, with a mean of 62.8%. In contrast, other IPF clinical trials, such as those for pirfenidone and nintedanib, have enrolled patients who on average had mild to moderate disease (mean FVC percent predicted 73.1% to 85.5%). Fourteen patients in Cohort 1 withdrew, and ten of the 14 had severe disease.

In order to enroll IPF patients similar to those in other IPF trials, we amended the protocol for Cohort 2 to include only patients with mild to moderate disease (FVC \geq 55% predicted). Baseline FVC percent predicted for Cohort 2 was 53% to 112%, with a mean of 72.7%. Based on this definition of disease severity, 37 patients in Cohort 1 and 32 patients in Cohort 2 had mild to moderate disease.

The table below provides a summary of the observed quantitative change in fibrosis for mild to moderate patients in Cohorts 1 and 2 as measured by quantitative HRCT. Twenty-four percent of these patients had improved fibrosis at Week 48. We believe that this is the first trial to demonstrate a reversal of fibrosis (as measured by HRCT) in a subset of IPF patients. Stable fibrosis has been considered the only achievable favorable outcome in IPF. The table below sets forth the number of patients who showed stable or improved fibrosis at Weeks 24 and 48 compared to the amount of fibrosis at the start of the trial.

Changes in Fibrosis in Patients with Mild to Moderate IPF Treated with Pamrevlumab in FGCL-3019-049

	Stable or Improved Compared to Baseline		Improved Compared to Baseline		Compared to Week 24
	Week 24	Week 48	Week 24	Week 48	Week 48
Cohort 1	21/45 (47%)	14/38 (37%)	12/45 (27%)	12/38 (32%)	8/38 (21%)
Cohort 2	12/29 (41%)	9/28 (32%)	5/29 (17%)	4/28 (14%)	8/26 (31%)
Combined	33/75 (44%)	23/66 (35%)	17/74 (23%)	16/66 (24%)	16/64 (25%)

Eighty-nine patients had at least one adverse event. The most common reported events were cough, fatigue, shortness of breath, upper respiratory tract infection, sore throat, bronchitis, nausea, dizziness, and urinary tract infection. Including the open-label extension, there were 45 serious adverse events in 31 patients, four of which were considered possibly related by the principal investigator to the investigational drug. After investigation, it is our belief that there is no causal relationship between pamrevlumab and the serious adverse events deemed possibly related by the principal investigator. During the first year of treatment there were 38 treatment-emergent serious adverse events in 24 patients. Adverse events observed to date are consistent with typical conditions observed in this patient population.

Pancreatic Cancer

Understanding Pancreatic Cancer and the Limitations of Current Therapies

Certain solid malignant tumors have a prominent fibrosis component consisting mostly of ECM that contributes to metastasis and progressive disease. ECM is the connective tissue framework of an organ or tissue.

Pancreatic ductal adenocarcinoma, or pancreatic cancer, is the third leading cause of cancer deaths in the U.S. According to the European Commission's European Cancer Information System, there were 100,005 new cases of pancreatic cancer and 95,373 deaths from pancreatic cancer in the Europe projected for 2018. The National Cancer Center of Japan estimated that there were 36,239 new cases of pancreatic cancer in 2014, increased from 24,442 cases in 2004. In its report of December 2017, Decision Resources Group estimated that the major market sales (U.S., Europe and Japan) of pancreatic cancer drugs will grow from \$1.3 billion in 2016 to approximately \$3.7 billion in 2026. According to the U.S. National Cancer Institute, there were an estimated 57,000 new cases of pancreatic cancer in the U.S. in 2019. Fifty percent of new cases are metastatic. Another 15-20% have localized resectable tumors. The remaining 30-35% have localized but unresectable tumors.

For those with non-resectable tumors, median survival is eight to 12 months post-diagnosis, and about 8% realize five years of survival; similar to metastatic cases. For those with resectable tumors, 50% survive 17 to 27 months post-diagnosis and ~20% report five-year survival.

Pancreatic cancer is aggressive and typically not diagnosed until it is largely incurable. Most patients are diagnosed after the age of 45, and according to the American Cancer Society, 94% of patients die within five years from diagnosis. The majority of patients are treated with chemotherapy, but pancreatic cancer is highly resistant to chemotherapy. Approximately 15% to 20% of patients are treated with surgery; however, even for those with successful surgical resection, the median survival is approximately two years, with a five year survival rate of 15% to 20% (Neesse et al. Gut (2011)). Radiation treatment may be used for locally advanced diseases, but it is not curative.

The duration of effect of approved anti-cancer agents to treat pancreatic cancer is limited. Gemcitabine demonstrated improvement in median overall survival from approximately four to six months, and erlotinib in combination with gemcitabine demonstrated an additional ten days of survival. Nab-paclitaxel in combination with gemcitabine was approved by the FDA in 2013 for the treatment of pancreatic cancer, having demonstrated median survival of 8.5 months. The combination of folinic acid, 5-fluorouracil, irinotecan and oxaliplatin (FOLFIRINOX) was reported to increase survival to 11.1 months from 6.8 months with gemcitabine. These drugs illustrate that progress in treatment for pancreatic cancer has been modest, and there remains a need for substantial improvement in patient survival and quality of life.

The approved chemotherapeutic treatments for pancreatic cancer target the cancer cells themselves. Tumors are composed of cancer cells and associated non-cancer tissue, or stroma, of which ECM is a major component. In certain cancers such as pancreatic cancer, both the stroma and tumor cells produce CTGF which in turn promotes the proliferation and survival of stromal and tumor cells. CTGF also induces ECM deposition that provides advantageous conditions for tumor cell adherence and proliferation, promotes blood vessel formation, or angiogenesis, and promotes metastasis, or tumor cell migration, to other parts of the body.

Pancreatic cancers are generally resistant to powerful chemotherapeutic agents, and there is now growing interest in the use of an anti-fibrotic agent to diminish the supportive role of stroma in tumor cell growth and metastasis. The anti-tumor effects observed with pamrevlumab in preclinical models indicate that it has the potential to inhibit tumor expansion through effects on tumor cell proliferation and apoptosis as well as reduce metastasis.

Phase 3 Clinical Development - Randomized, Double-Blind, Placebo-Controlled Trial of Pamrevlumab in Locally Advanced, Unresectable Pancreatic Cancer

We continue to enroll LAPIS, our double-blind placebo controlled Phase 3 trial of pamrevlumab as a neoadjuvant therapy for locally advanced unresectable pancreatic cancer. We intend to enroll approximately 260 patients, randomized 1:1 to receive either pamrevlumab, in combination with gemcitabine and nab-paclitaxel, or placebo with gemcitabine and nab-paclitaxel. After completion of the 6-month treatment period, if the results show an improved resection rate in the pamrevlumab arm, we may request a meeting with the FDA to discuss the adequacy of these results to support a marketing application under the provisions of accelerated approval. After this interim assessment of resection rates, the study will continue to collect data on overall survival, the primary endpoint.

Study 069 - Randomized, Open-Label, Active-Controlled Phase 1/2 Trial of Pamrevlumab in Locally Advanced Pancreatic Cancer

We continue to follow patients in our ongoing open-label, randomized (2:1) Phase 1/2 trial (FGC004C-3019-069) of pamrevlumab combined with gemcitabine plus nab-paclitaxel chemotherapy vs. the chemotherapy regimen alone in patients with inoperable locally advanced pancreatic cancer that has not been previously treated. We enrolled 37 patients in this study and completed the six-month treatment period and surgical assessment at the end of 2017. The overall goal of the trial is to determine whether the pamrevlumab combination can convert inoperable pancreatic cancer to operable, or resectable, cancer. Tumor removal is the only chance for cure of pancreatic cancer, but only approximately 15% to 20% of patients are eligible for surgery.

We reported updated results from this ongoing study at the American Society of Clinical Oncology Annual Meeting in June 2018. A higher proportion (70.8%) of pamrevlumab-treated patients whose tumors were previously considered unresectable became eligible for surgical exploration than patients who received chemotherapy alone (15.4%), based on pre-specified eligibility criteria at the end of 6 months of treatment. Furthermore, a higher proportion of pamrevlumab-treated patients (33.3%) achieved surgical resection than those who received chemotherapy alone (7.7%).

In addition, this data showed improved overall survival among patients who were resected vs. not resected (NE vs. 18.56 months, p-value=0.0141) and a trend toward improved overall survival in patients eligible for surgery vs. patients who were not (27.73 vs. 18.40 months, p-value=0.0766). All of the patients on study at the time of the results reported in June 2018 continue to remain on study. No increase in serious adverse events was observed in the pamrevlumab arm and no delay in wound healing was observed post-surgery.

Patients with locally advanced unresectable pancreatic cancer have median survival of less than 12 months, only slightly better than patients with metastatic pancreatic cancer, whereas patients with resectable pancreatic cancer have a much better prognosis with median survival of approximately 23 months and some patients being cured. If pamrevlumab in combination with chemotherapy continues to demonstrate an enhanced rate of conversion from unresectable cancer to resectable cancer, it may support the possibility that pamrevlumab could provide a substantial survival benefit for locally advanced pancreatic cancer patients.

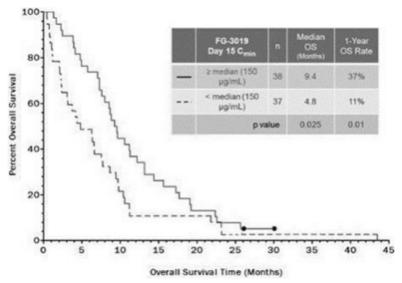
Completed Clinical Trials of Pamrevlumab in Pancreatic Cancer

We completed an open-label Phase 1/2 (FGCL-MC3019-028) dose finding trial of pamrevlumab combined with gemcitabine plus erlotinib in patients with previously untreated locally advanced (Stage 3) or metastatic (Stage 4) pancreatic cancer. These study results were published in the *Journal of Cancer Clinical Trials* (Picozzi et al., J Cancer Clin Trials 2017, 2:123). Treatment continued until progression of the cancer or the patient withdrew for other reasons. Patients were then followed until death.

Seventy-five patients were enrolled in this study with 66 (88%) having Stage 4 metastatic cancer. The study demonstrated a dose-related increase in survival. At the lowest doses, no patients survived for even one year while at the highest doses up to 31% of patients survived one year.

A post-hoc analysis found that there was a significant relationship between survival and trough levels of plasma pamrevlumab measured immediately before the second dose (Cmin), as illustrated below. Cmin greater than or equal to $150~\mu g/mL$ was associated with significantly improved progression-free survival (p=0.01) and overall survival (p=0.03) vs. those patients with Cmin less than $150~\mu g/mL$. For patients with Cmin >150 $\mu g/mL$ median survival was 9.0 months compared to median survival of 4.4 months for patients with Cmin <150 $\mu g/mL$. Similarly, 34.2% of patients with Cmin >150 $\mu g/mL$ survived for longer than one year compared to 10.8% for patients with Cmin <150 $\mu g/mL$. These data suggest that sufficient blockade of CTGF requires pamrevlumab threshold blood levels of approximately $150~\mu g/mL$ in order to improve survival in patients with advanced pancreatic cancer.

Increased Pancreatic Cancer Survival Associated with Increased Plasma Levels of Pamrevlumab



The Kaplan-Meier plot provides a representation of survival of all patients in the clinical trial. Each vertical drop in the curve represents a recorded event (death) of one or more patients. When a patient's event cannot be determined either because he or she has withdrawn from the study or because the analysis is completed before the event has occurred, that patient is "censored" and denoted by a symbol (•) on the curve at the time of the last reliable assessment of that patient.

In the study, the majority of adverse events were mild to moderate, and were consistent with those observed for erlotinib plus gemcitabine treatment without pamrevlumab. There were 99 treatment-emergent serious adverse events; six of which were assessed as possibly related to the investigational drug by the principal investigator, and 93 as not related to study treatment. After investigation, it is our belief that there is no causal relationship between pamrevlumab and the treatment-emergent serious adverse events deemed possibly related by the principal investigator. We did not identify any evolving dose-dependent pattern, and higher doses of pamrevlumab were not associated with higher numbers of serious adverse events or greater severity of the serious adverse events observed.

Pamrevlumab for Duchenne Muscular Dystrophy

Understanding DMD and the Limitations of Current Therapies

In the U.S., approximately one in every 5,000 boys have DMD, and approximately 20,000 children are diagnosed with DMD globally each year. There are currently no approved disease-modifying treatments. Despite taking steroids to mitigate progressive muscle loss, a majority of children with DMD are non-ambulatory by adolescence, and median survival is age 25.

DMD is an inherited disorder of one of the dystrophin genes resulting in absence of the dystrophin protein and abnormal muscle structure and function, leading to progressively diminished mobility as well as pulmonary function and cardiac function which result in early death. Constant myofiber breakdown results in persistent activation of myofibroblasts and altered production of ECM resulting in extensive fibrosis in skeletal muscles of DMD patients. Desguerre et al. (2009) showed that muscle fibrosis was the only myo-pathologic parameter that significantly correlated with poor motor outcome as assessed by quadriceps muscle strength, manual muscle testing of upper and lower limbs, and age at ambulation loss. Numerous pre-clinical studies including those in the mdx model of DMD suggest that CTGF contributes to the process by which muscle is replaced by fibrosis and fat and that CTGF may also impair muscle cell differentiation during muscle repair after injury.

Clinical Development of Pamrevlumab for Duchenne Muscular Dystrophy

Based on the FDA review of one year data from our Phase 2 administrative analysis, we intend to begin a Phase 3 study of pamrevlumab in non-ambulatory DMD patients in the second half of 2020.

All 21 non-ambulatory patients from our fully enrolled Phase 2 open-label single-arm trial have completed over one year of treatment with pamrevlumab. While we cannot make direct comparisons between our trial and previously published data due to, among other things, differences in subject numbers, baseline characteristics, inclusion/exclusion criteria, treatment protocols, and analysis methods, we are encouraged by the data obtained so far. Pamrevlumab was well tolerated in this study.

In June 2019 at the Parent Project Muscular Dystrophy meeting, we reported topline results from our one-year administrative analysis comparing our Phase 2 data to recent published natural disease history studies of DMD patients.

In pulmonary function tests, the results from our study indicate a potential reduction in the 1-year decline in FVC percent predicted from baseline for our pamrevlumab-treated patients when compared to FVC data of DMD patients (whether such patients were taking steroids or not) published in 2019 by Ricotti. In the 2019 Ricotti study, the DMD patients were treated with steroids only. Similarly, all of the patients in our Phase 2 pamrevlumab trial were on steroids. In addition, pamrevlumab showed less decline in both percent predicted forced expiratory volume as compared to previously published study results of Meier in 2016, and in percent predicted peak expiratory flow rate, compared to what was observed in the study by Ricotti in 2019.

Our data showed an increase in cardiac function, measured by mean change of left ventricular ejection fraction ("LVEF"), of 0.29% from baseline for our pamrevlumab-treated patients. Whereas, data published in 2018 by McDonald of DMD patients only on steroids showed a mean LVEF decline of 0.82% from baseline in one year.

In muscle function tests, the majority of the results of this Phase 2 study showed the mean change from baseline in our pamrevlumab-treated patients were more favorable than previously published data. Our results showed a positive increase in grip-strength score in both dominant and non-dominant hands at one year of treatment with pamrevlumab, while earlier results from a 2015 study by Seferian showed a decline at one year as expected. In the performance of the upper limb ("PUL") test specifically developed for DMD patients, our pamrevlumab-treated patients had a mean change from baseline of -1.53. In the 2019 study by Ricotti of DMD patients taking either nothing or only steroids, the annual mean change in the PUL test was -4.13. Furthermore, in our study a strong correlation between change in biceps brachii T2-mapping and change in PUL score was observed, demonstrating stabilization and even possible improvement in the muscle fibrosis burden.

Commercialization Strategy for Pamrevlumab

Our goal, if pamrevlumab is successful, is to be a leader in the development and commercialization of novel approaches for inhibiting fibrosis and treating some forms of cancer and muscular dystrophy diseases. To date, we have retained exclusive worldwide rights for pamrevlumab.

COLLABORATIONS

Collaboration Partnerships for Roxadustat

Astellas

We have two agreements with Astellas for the development and commercialization of roxadustat, one for Japan, and one for Europe, the Commonwealth of Independent States, the Middle East and South Africa. Under these agreements we provided Astellas the right to develop and commercialize roxadustat for anemia in these territories.

We share responsibility with Astellas for clinical development activities required for U.S. and Europe regulatory approval of roxadustat, and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will own and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

The Astellas agreements will continue in effect until terminated. Either party may terminate the agreements for certain material breaches by the other party. In addition, Astellas will have the right to terminate the agreements for certain specified technical product failures, upon generic sales reaching a particular threshold, upon certain regulatory actions, or upon our entering into a settlement admitting the invalidity or unenforceability of our licensed patents. Astellas may also terminate the agreements for convenience upon advance written notice to us. In the event of any termination of the agreements, Astellas will transfer and assign to us the regulatory filings for roxadustat and will assign or license us the relevant trademarks used with the products in the Astellas territories. Under certain terminations, Astellas is also obligated to pay us a termination fee.

Consideration under these agreements includes a total of \$360.1 million in upfront and non-contingent payments, and milestone payments totaling \$557.5 million, of which \$542.5 million are development and regulatory milestones, and \$15.0 million are commercial-based milestones. Total consideration, excluding development cost reimbursement and product sales-related payments, could reach \$917.6 million.

Additionally, under these agreements, Astellas pays 100% of the commercialization costs in their territories. Astellas will pay us a transfer price for our manufacture and delivery of roxadustat based on net sales of roxadustat in the low 20% range.

AstraZeneca

We also have two agreements with AstraZeneca for the development and commercialization of roxadustat for anemia, one for China (the "China Agreement"), and one for the U.S. and all other countries not previously licensed to Astellas (the "U.S./RoW Agreement"). Under these agreements we provided AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories. We share responsibility with AstraZeneca for clinical development activities required for U.S. regulatory approval of roxadustat.

In 2015, we reached the \$116.5 million cap on our initial funding obligations (under which we shared 50% of the initial development costs), therefore all future development and commercialization costs for roxadustat for the treatment of anemia in CKD in the U.S., Europe, Japan and all other markets outside of China will be paid by Astellas and AstraZeneca.

In China, our subsidiary FibroGen Beijing will conduct the development work for CKD anemia and will hold all of the regulatory licenses issued by China regulatory authorities and be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is also responsible for 100% of development expenses in all other licensed territories outside of China. We are responsible, through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

Under the AstraZeneca agreements, we receive upfront and subsequent non-contingent payments totaling \$402.2 million. Potential milestone payments under the agreements total \$1.2 billion, of which \$571.0 million are development and regulatory milestones, and \$652.5 million are commercial-based milestones. Total consideration under the agreements, excluding development cost reimbursement, transfer price payments, royalties and profit share, could reach \$1.6 billion.

Payments under these agreements include over \$500 million in upfront, non-contingent and other payments received or expected to be received prior to the first U.S. approval, excluding development expense reimbursement.

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Under the U.S./RoW Agreement, AstraZeneca will pay for all commercialization costs in the U.S. and RoW, AstraZeneca will be responsible for the U.S. commercialization of roxadustat, with FibroGen undertaking specified promotional activities in the ESRD segment in the U.S. In addition, we will receive a transfer price for delivery of commercial product based on a percentage of net sales in the low- to mid-single digit range and AstraZeneca will pay us a tiered royalty on net sales of roxadustat in the low 20% range.

Under the China Agreement, which is conducted through FibroGen China Anemia Holdings, Ltd. ("FibroGen China"), the commercial collaboration is structured as a 50/50 profit share. AstraZeneca will conduct sales and marketing activities in China for roxadustat and will fund roxadustat launch costs in China until FibroGen Beijing has achieved profitability. At that time, AstraZeneca will recoup 50% of their historical launch costs out of initial roxadustat profits in China.

AstraZeneca may terminate the U.S./RoW Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon 180 days prior written notice at will. If AstraZeneca terminates the U.S/RoW Agreement at will, in addition to any unpaid non-contingent payments, it will be responsible to pay for a substantial portion of the post-termination development costs under the agreed development plan until regulatory approval.

AstraZeneca may terminate the China Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon advance prior written notice at will. If AstraZeneca terminates our China Agreement at will, it will be responsible to pay for transition costs as well as make a specified payment to FibroGen China.

In the event of any termination of the agreements, but subject to modification upon termination for technical product failure, AstraZeneca will transfer and assign to us any regulatory filings and approvals for roxadustat in the affected territories that they may hold under our agreements, grant us licenses and conduct certain transition activities.

Additional Information Related to Collaboration Agreements

Additional information related to collaboration agreements is set forth in Item 7 of this Annual Report on Form 10-K. Information about collaboration partners that accounted for more than 10% of our total revenue or accounts receivable for the last three fiscal years is set forth in Note 14 to our consolidated financial statements under Item 8 of this Annual Report.

COMPETITION

The pharmaceutical and biotechnology industries are highly competitive, particularly in some of the indications we are developing drug candidates, including anemia in CKD, IPF, pancreatic cancer, and DMD. We face competition from multiple other pharmaceutical and biotechnology companies, many of which have significantly greater financial, technical and human resources and experience in product development, manufacturing and marketing. These potential advantages of our competitors are particularly a risk in IPF, pancreatic cancer, and DMD, where we do not currently have a development or commercialization partner.

We expect any products that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition, and the availability of reimbursement from government and other third-party payors.

When any of our product candidates are approved, they will compete with currently marketed products, and product candidates that may be approved for marketing in the future, for treatment of the following indications:

Roxadustat - Anemia in CKD

Drugs that will compete with roxadustat are expected to include ESAs, particularly in those patient segments where ESAs are used. Currently available ESAs include epoetin alfa (EPOGEN® marketed by Amgen Inc. in the U.S., Procrit® and Erypo®/Eprex®, marketed by Johnson & Johnson, Inc. and Espo® marketed by Kyowa Hakko Kirin in Japan and China), darbepoetin (Amgen/Kyowa Hakko Kirin's Aranesp® and NESP®) and Mircera® marketed by Roche outside the U.S. and by Vifor Pharma ("Vifor"), a Roche licensee, in the U.S. and Puerto Rico, as well as biosimilar versions of these currently marketed ESA products. ESAs have been used in the treatment of anemia in CKD for more than 20 years, serving a significant majority of dialysis patients. While non-dialysis CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated, some patients under nephrology care may be receiving ESA therapy. It may be difficult to encourage healthcare providers and patients to switch to roxadustat from products with which they have become familiar.

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We may also face competition from potential new anemia therapies currently in clinical development, including in those patient segments not currently addressed by ESAs. Companies that are currently developing HIF-PH inhibitors for anemia in CKD indications include GlaxoSmithKline plc ("GSK"), Bayer Corporation ("Bayer"), Akebia Therapeutics, Inc. ("Akebia"), Japan Tobacco, and Zydus Cadila. Akebia is currently conducting Phase 3 studies in CKD patients on dialysis and not on dialysis, as well as a Phase 2 study evaluating pharmacokinetics and pharmacodynamics in dialysis-dependent patients with three-times weekly versus once-a-day dosing. Akebia expects to complete these studies by August 2020. In Japan, Mitsubishi Tanabe Pharmaceutical Corporation, Akebia's collaboration partner, submitted an NDA for treatment of anemia in dialysis and non-dialysis CKD patients in July 2019, and is awaiting an approval decision later in 2020. GSK is also conducting global Phase 3 studies in CKD patients on dialysis and not on dialysis, and expects to complete those studies by March 2022. GSK and Kyowa Hakko Kirin announced in November 2018 that the two companies signed a strategic commercialization deal in Japan for daprodustat. GSK submitted a Japan NDA for treatment of anemia in dialysis and non-dialysis in August 2019 and is awaiting approval later in 2020. Bayer has completed global Phase 2 studies and its HIF-PH inhibitor is now in Phase 3 development in CKD populations on dialysis and not on dialysis in Japan. Japan Tobacco submitted an NDA for treatment of anemia associated with CKD in Japan in November 2019, supported by the six Phase 3 studies conducted in CKD patients on dialysis and not on dialysis in Japan, and its partner JW Pharmaceuticals started a Phase 3 study in dialysis patients in Korea. Zydus Cadila (India) started Phase 3 studies in dialysis and non-dialysis CKD patients in India in 2019.

In addition, there are other companies developing biologic therapies for the treatment of other anemia indications that we may also seek to pursue in the future, including anemia of MDS. For example, Acceleron Pharma, Inc., in partnership with Celgene Corporation, a Bristol-Myers Squibb company ("Celgene"), developed Reblozyl® (luspatercept), a protein therapeutic, which was approved in November 2019 by the FDA for anemia treatment in patients with β-thalassemia. Its Biologics License Application ("BLA") under review by the FDA, for treatment of adult patients with very low to intermediate MDS associated anemia who have ring sideroblast and require red blood cell transfusions, has a Prescription Drug User Fee Act date of April 4, 2020. Acceleron expects an EMA decision on the MAA in the second half of 2020. In Japan, Celgene started a luspatercept Phase 2 study in May 2019. We may face competition for patient recruitment, enrollment for clinical trials, and potentially in commercial sales. There may also be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat if and when it is commercialized.

In China, biosimilars of epoetin alfa are offered by Chinese pharmaceutical companies such as EPIAO marketed by 3SBio Inc. as well as more than 15 other local manufacturers. We may also face competition by HIF-PH inhibitors from other companies such as Akebia, Bayer, and GSK, which was authorized by the National Medical Products Administration ("NMPA") to conduct trials in China to support its ex-China regulatory filings. Two domestic companies, Jiangsu Hengrui Medicine Co., Ltd. and Guandong Sunshine Health Investment Co., Ltd, have been permitted by the NMPA to conduct clinical trials for CKD anemia patients both on dialysis and not on dialysis, and 3SBio Inc. has submitted a clinical trial application to the NMPA to initiate trials for their HIF-PH inhibitor. Another domestic company, China Medical System, in-licensed desidustat, a compound which is currently in Phase 3 trials in India, from Zydus Candila for greater China in January 2020. Akebia announced in December 2015 that it had entered into a development and commercialization partnership with Mitsubishi Tanabe Pharmaceutical Corporation for its HIF-PH inhibitor vadadustat in Japan, Taiwan, South Korea, India and certain other countries in Asia, and announced in April 2017 an expansion of their U.S. collaboration with Otsuka to add markets, including China. 3SBio Inc. announced in 2016 its plan to begin a Phase 1 clinical trial of a HIF-PH inhibitor for the China market.

The first biosimilar ESA, Pfizer's Retacrit® (epoetin zeta), entered the U.S. market in November 2018. Market penetration of Retacrit and the potential addition of other biosimilar ESAs currently under development may alter the competitive and pricing landscape of anemia therapy in CKD patients on dialysis under the ESRD bundle. The patents for Amgen's EPOGEN® (epoetin alfa) expired in 2004 in the Europe, and the final material patents in the U.S. expired in May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in the Europe, China and other territories. In the U.S., a few ESA biosimilars are currently under development. Sandoz, a division of Novartis, markets Binocrit® (epoetin alfa) in Europe and may file a biosimilar BLA in the U.S.

The majority of the current CKD anemia market focuses on dialysis patients, who visit dialysis centers on a regular basis, typically three times a week, and anemia therapies are administered as part of the visit. Two of the largest operators of dialysis clinics in the U.S., DaVita Healthcare Partners Inc. ("DaVita"), and Fresenius Medical Care AG & Co. KGaA ("Fresenius"), collectively provide dialysis care to more than 80% of U.S. dialysis patients, and therefore have historically won long-term contracts including rebate terms with Amgen. DaVita has a six-year sourcing and supply agreement with Amgen effective through 2022. Fresenius' contract with Amgen expired in 2015, following which Fresenius is providing Roche's ESA Mircera® to a significant portion of its U.S. dialysis patients. Successful penetration in this market may require a significant agreement with Fresenius or DaVita, on favorable terms and on a timely basis.

Pamrevlumab

We are currently in Phase 2 development of pamrevlumab to treat DMD and Phase 3 development of pamrevlumab in IPF and pancreatic cancer. Most of our competitors have significantly more resources and expertise in development, commercialization and manufacturing, particularly due to the fact that we have not yet established a co-development partnership for pamrevlumab. For example, both Roche and Boehringer Ingelheim, which market products for the treatment of IPF in the U.S., have successfully developed and commercialized drugs in various indications and have built sales organizations that we do not currently have; both have more resources and more established relationships when competing with us for patient recruitment and enrollment for clinical trials or, if we are approved, in the market.

Idiopathic Pulmonary Fibrosis

If approved and launched commercially to treat IPF, pamrevlumab is expected to compete with Roche's Esbriet® (pirfenidone), and Boehringer Ingelheim's Ofev® (nintedanib). We believe that if pamrevlumab can be shown to safely stabilize or reverse lung fibrosis, and thus stabilize or improve lung function in IPF patients, it can compete with pirfenidone and nintedanib for market share in IPF. However, it may be difficult to encourage treatment providers and patients to switch to pamrevlumab from a product they are already familiar with. We may also face competition from potential new IPF therapies in recruitment and enrollment in our clinical trials and potentially in commercialization.

Pamrevlumab is an injectable protein, which may be more expensive and less convenient than small molecules such as nintedanib and pirfenidone. Other potential competitive product candidates in various stages of development for IPF include Galapagos NV's GLPG1690 and GLPG1205, Kadmon Holdings, Inc.'s KD025, Liminal BioSciences' PBI-4050, and Roche/Promedior, Inc.'s PRM-151. In particular, GLPG1690 is in a Phase 3 program consisting of two clinical trials with 750 subjects each, intended to support both the U.S. NDA and MAA in Europe.

Pancreatic Cancer

We are developing pamrevlumab to be used in combination with Abraxane® (nab-paclitaxel) and gemcitabine in pancreatic cancer. Celgene's Abraxane was launched in the U.S. and Europe in 2013 and 2014, respectively, and was the first drug approved in this disease in nearly a decade. In 2015, Merrimack Pharmaceuticals Inc. ("Merrimack") received FDA approval for the use of ONIVYDE (irinotecan liposome injection, now licensed to Ipsen) for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy, and the combination therapy with Abraxane and gemcitabine became the first-line standard of care in these patients. As treatments for pancreatic cancer have shown limited success to date, combination therapies are expected, but the incremental cost may slow a new product adoption in the market, at least until the generic versions of Abraxane becomes available. In addition, we may also face competition from other products seeking approval in conjunction with gemcitabine and Abraxane including FOLFRINOX, a combination chemotherapy regimen of folic acid, 5-fluouracil, oxaliplatin and irinotecan, Rafael Pharma's defactinib/CPI-613, and Merrimack's istiratumab.

Duchenne Muscular Dystrophy

If approved and launched commercially to treat DMD, pamrevlumab is expected to face competition from drugs that have been approved in major markets such as the U.S., EU, and Japan.

On September 19, 2016, the FDA approved Sarepta Therapeutics Inc.'s ("Sarepta") Exondys 51TM (eteplirsen). This was the first drug approved to treat DMD. Exondys 51 is approved to treat patients who have a mutation of the dystrophin gene amenable to exon 51 skipping, representing approximately 13% of patients with DMD. In Europe, Sarepta received a negative opinion for its marketing application for eteplirsen from the EMA in September 2018. Sarepta has reported a full year Exondys 51 revenue of \$380 million in 2019. Sarepta's Vyondys 53TM (golodirsen) was also approved by the FDA in December 2019 for patients with a confirmed genetic mutation that is amenable to exon 53 skipping, which accounts for 8% of the DMD population.

PTC Therapeutics' product Translarna TM received a conditional approval in Europe in 2014, which was renewed in November 2016 with a request for a new randomized placebo-controlled 18-month study by the Committee for Medicinal Products for Human Use of the EMA; however, the FDA informed the sponsor in a complete response letter in October 2017, as well as in its response to PTC Therapeutics' appeal, that the FDA is unable to approve the application in its current form. While Translarna TM targets a different set of DMD patients from those targeted by Sarepta's Exondys 51®, it is also limited to a subset of patients who carry a specific mutation. Conversely, pamrevlumab is intended to treat DMD patients without limitation to type of mutation.

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Pamrevlumab may also face competition from other drugs currently in clinical development in patient recruiting and enrollment in clinical trials, and, if approved, in commercialization. Examples of those compounds currently under clinical development are the drug candidates from Catabasis Pharmaceuticals ("Catabasis"), Santhera Pharmaceuticals ("Santhera") and Sarepta. Catabasis' edasalonexent was reported to have preserved muscle function and slowed the progression of DMD compared to rates of change in the control period prior to treatment with edasalonexent in a Phase 2 study, and is currently undergoing Phase 3 development. Santhera's Puldysa® (idebenone) MAA for treatment of DMD was filed with the EMA, and the opinion from the Committee for Medicinal Products for Human Use is expected in the second quarter of 2020. The FDA requested additional clinical data from the idebenone Phase 3 trial currently ongoing in the U.S. and Europe. Santhera offers compassionate use of idebenone in patients with DMD in U.S. and UK. Sarepta's SRP-9001 is an investigational gene therapy for DMD. Sarepta announced in December 2019 the licensing agreement with Roche that grants Roche the commercial rights to SRP-9001 outside the U.S.

MANUFACTURE AND SUPPLY

We have historically and in the future plan to continue to enter into contractual arrangements with qualified third-party manufacturers to manufacture and package our products and product candidates. We believe that this manufacturing strategy enables us to more efficiently direct financial resources to the research, development and commercialization of product candidates rather than diverting resources to establishing a significant internal manufacturing infrastructure, unless there is additional strategic value for establishing manufacturing capabilities, such as in China. As our product candidates proceed through development, we explore or enter into longer term commercial supply agreements with key suppliers and manufacturers in order to meet the ongoing and planned clinical and commercial supply needs for ourselves and our partners. Our timing of entry into these agreements is based on the current development and commercialization plans.

Roxadustat

Roxadustat is a small-molecule drug manufactured from generally available commercial starting materials and chemical technologies and multipurpose equipment available from many third party contract manufacturers. Outside of China, we plan to continue to use, Shanghai SynTheAll
Pharmaceutical Co., Ltd. ("WuXi STA") and Catalent, Inc. ("Catalent") as our primary manufacturers of roxadustat drug substance (also known as
active pharmaceutical ingredient or "API") and roxadustat drug product, respectively. WuXi STA is located in China and currently supplies our API
globally except for China, for which it manufactures an intermediate to be further manufactured by FibroGen China. WuXi STA has passed
inspections by several regulatory agencies, including the FDA and NMPA, and is Current Good Manufacturing Practice ("cGMP") compliant.
Catalent is located in the U.S. and supplies our drug product tablets globally except for Japan, where they are manufactured by Astellas, and China,
where they are manufactured by FibroGen China. Catalent has passed several regulatory inspections, including by the FDA, and manufactures
commercial products for other clients.

To date, we believe that roxadustat has been manufactured under cGMP and in compliance with applicable regulatory requirements for the manufacture of drug substance and drug product used in clinical trials and we and Astellas have performed audits of the existing roxadustat manufacturers. The intended commercial manufacturing route outside of China has been successfully scaled up to multiple hundred kilogram scale and produced several metric tons of roxadustat drug substance. We are in discussions with multiple parties regarding longer term commercial supply arrangements.

In China, our Beijing facility received the Good Manufacturing Practice ("GMP") license for API and drug product. We are manufacturing drug product at our FibroGen Beijing manufacturing facility for commercial supply. We are manufacturing API at our Cangzhou manufacturing facility, which has been fully qualified and licensed. We may also qualify a third party manufacturer to produce commercial API under the Marketing Authorization Holder System program.

Irix Pharmaceuticals, Inc.

In July 2002, we and IRIX Pharmaceuticals, Inc. ("IRIX"), a third party manufacturer, entered into a Letter of Agreement for IRIX Pharmaceuticals Single Source Manufacturing Agreement (the "Letter of Agreement"), in connection with a contract manufacturing arrangement for clinical supplies of HIF-PH inhibitors, including roxadustat. The Letter of Agreement contained a service agreement that included terms and schedule for the delivery of clinical materials, and also included a term sheet for a single source agreement for the cGMP manufacture of HIF-PH inhibitors, including roxadustat. Specifically, pursuant to the Letter of Agreement, we and IRIX agreed to negotiate a single source manufacturing agreement that included a first right to negotiate a manufacturing contract for HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third party bids within 5%, and the exclusive right to manufacture extends for five years after approval of an NDA. Any agreement would provide that no minimum amounts would be specified until appropriate by forecast, that we and our commercialization partner would have the rights to contract with independent third parties that exceed IRIX's internal capabilities or in the event that we or our commercialization partner determines for reasons of continuity and security that such a need exists, provided that IRIX would supply a majority of the product if it is able to meet the requirements and the schedule required by us and our partner. Subsequent to the Letter of Agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the Letter of Agreement with respect to the single source manufacturing agreement. To date, we have offered to IRIX opportunities to bid for the manufacture of HIF-PH inhibitors, including roxadustat. In 2015, Patheon Pharmaceuticals Inc., a business unit of DPx Holdings B.V. ("Patheon"), acquired IRIX, and in 2017 ThermoFisher Scientific Inc. acquired Patheon.

Pamreylumab

To date, pamrevlumab has been manufactured using specialized biopharmaceutical process techniques under an agreement with a qualified third party contract manufacturer, Boehringer Ingelheim. Our contract manufacturer is the sole source for the current clinical supply of the drug substance and drug product for pamrevlumab. Our contract manufacturer is only obligated to supply the amounts of pamrevlumab as agreed on pursuant to work orders that are executed from time to time under our agreement as we determine need for clinical material, and we are not required to make fixed or minimum annual purchases. Our existing agreement allows us to transfer the cell line manufacturing process to another third party manufacturer at our expense, and our contractor is obligated to provide reasonable technology transfer assistance in the event of such a transfer.

GOVERNMENT REGULATION

The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the U.S. and other countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations, including in Europe and China, requires the expenditure of substantial time and financial resources. Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the applicable regulatory authority to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by FDA and the Department of Justice, or other governmental entities.

U.S. Product Approval Process

In the U.S., the FDA regulates drugs and biological products, or biologics, under the Public Health Service Act, as well as the FDCA which is the primary law for regulation of drug products. Both drugs and biologics are subject to the regulations and guidance implementing these laws. Pharmaceutical products are also subject to regulation by other governmental agencies, such as the Federal Trade Commission, the Office of Inspector General of the U.S. Department of Health and Human Services, the Consumer Product Safety Commission and the Environmental Protection Agency. The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the U.S. and other countries. The steps required before a drug or biologic may be approved for marketing in the U.S. generally include:

- Preclinical laboratory tests and animal tests conducted under Good Laboratory Practices.
- The submission to the FDA of an IND for human clinical testing, which must become effective before each human clinical trial commence.
- Adequate and well-controlled human clinical trials to establish the safety and efficacy of the product and conducted in accordance with Good Clinical Practices.

- The submission to the FDA of an NDA, in the case of a small molecule drug product, or a BLA, in the case of a biologic product.
- FDA acceptance, review and approval of the NDA or BLA, as applicable.
- Satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. The FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to a potentially unacceptable health risk.

Preclinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. Preclinical studies must be conducted in compliance with FDA regulations regarding GLPs. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which includes the results of preclinical testing and a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase or phases of the clinical trial lends themselves to an efficacy determination. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. The IND must become effective before clinical trials may be commenced.

Clinical trials involve the administration of the product candidates to healthy volunteers, or subjects, or patients with the disease to be treated under the supervision of a qualified principal investigator. Clinical trials must be conducted under the supervision of one or more qualified principal investigators in accordance with GCPs and in accordance with protocols detailing the objectives of the applicable phase of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Progress reports detailing the status of clinical trials must be submitted to the FDA annually. Sponsors must also timely report to the FDA serious and unexpected adverse events, any clinically important increase in the rate of a serious suspected adverse event over that listed in the protocol or investigator's brochure, or any findings from other studies or tests that suggest a significant risk in humans exposed to the product candidate. Further, the protocol for each clinical trial must be reviewed and approved by an independent institutional review board ("IRB"), either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, ethical factors, and the safety of human subjects and the possible liability of the institution.

Clinical trials are typically conducted in three sequential phases prior to approval, but the phases may overlap and different trials may be initiated with the same drug candidate within the same phase of development in similar or different patient populations. These phases generally include the following:

Phase 1. Phase 1 clinical trials represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for pharmacodynamic and pharmacokinetic properties such as safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism and excretion.

Phase 2. Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the product candidate for specific indications, (2) determine dosage tolerance and optimal dosage and (3) identify possible adverse effects and safety risks.

Phase 3. If a product candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 studies, the clinical trial program will be expanded to Phase 3 clinical trials to further evaluate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical study sites.

Phase 4. Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of approval.

The results of preclinical studies and clinical trials, together with detailed information on the manufacture, composition and quality of the product candidate, are submitted to the FDA in the form of an NDA (for a drug) or BLA (for a biologic), requesting approval to market the product. The application must be accompanied by a significant user fee payment. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

Review of Application

Once the NDA or BLA submission has been accepted for filing, which occurs, if at all, 60 days after submission, the FDA informs the applicant of the specific date by which the FDA intends to complete its review. This is typically 12 months from the date of submission. The review process is often extended by FDA requests for additional information or clarification. The FDA reviews NDAs and BLAs to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA or BLA, the FDA may inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and will also inspect clinical trial sites for integrity of data supporting safety and efficacy. During the approval process, the FDA also will determine whether a REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS; the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA will issue either an approval of the NDA or BLA or a complete response letter detailing the deficiencies and information required in order for reconsideration of the application.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act, certain drugs or biologics may obtain an additional six months of exclusivity in an indication, if the sponsor submits information requested in writing by the FDA ("Written Request"), relating to the use of the active moiety of the drug or biologic in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug or biologic in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not received a Written Request for such pediatric studies with respect to our product candidates, although we may ask the FDA to issue a Written Request for studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and submit reports of the studies. A Written Request may include studies for indications that are not currently in the labeling if the FDA determines that such information will benefit the public health. The FDA will accept the reports upon its determination that the studies were conducted in accordance with and are responsive to the original Written Request, agreement, or commonly accepted scientific principles, as appropriate, and that the reports comply with the FDA's filing requirements.

In addition, the Pediatric Research Equity Act ("PREA") requires a sponsor to conduct pediatric studies for most drugs and biologicals, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must include the evaluation of the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA, on its own initiative or at the request of the sponsor, may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted by FDA if they believe that additional safety or effectiveness data in the adult population needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Post-Approval Requirements

Even after approval, drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to continuous regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, entities involved in the manufacture and distribution of approved drugs and biologics are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may also result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- · Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls.
- Fines, warning letters or holds on post-approval clinical trials.
- Refusal of the FDA to approve pending NDAs or BLAs or supplements to approved NDAs or BLAs, or suspension or revocation of
 product license approvals.
- Product seizure or detention, or refusal to permit the import or export of products.
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Prescription Drug Marketing Act

The distribution of pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors at the state level. Under the PDMA and state law, states require the registration of manufacturers and distributors who provide pharmaceuticals in that state, including in certain states manufacturers and distributors who ship pharmaceuticals into the state even if such manufacturers or distributors have no place of business within the state. The PDMA and state laws impose requirements and limitations upon drug sampling to ensure accountability in the distribution of samples. The PDMA sets forth civil and criminal penalties for violations of these and other provisions.

Federal and State Fraud and Abuse and Data Privacy and Security and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the biopharmaceutical industry. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

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The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for a statutory exception or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010 (collectively "PPACA"), to a stricter intent standard such that a person or entity no longer needs to have actual knowledge of this statute or the specific intent to violate it in order to have committed a violation. In addition, PPACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below). Further, civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses. The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates - independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act within the PPACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some states require the posting of information relating to clinical studies. In addition, California requires pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals. If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales of any approved products will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of our products will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by third-party payors. These third-party payors are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare product candidates. The market for our products and product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that our products and our product candidates will be considered cost-effective. Because coverage and reimbursement determinations are made on a payor-by-payor basis, obtaining acceptable coverage and reimbursement from one payor does not guarantee that we will obtain similar acceptable coverage or reimbursement from another payor. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success.

In addition, in many foreign countries, particularly the countries of the Europe and China, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the Europe provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of a company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the U.S. and foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to directly commercialize our products. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state level that seek to reduce healthcare costs. If a drug product is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA"). The MMA imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain from non-governmental payors. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payors.

Moreover, on November 27, 2013, the federal Drug Supply Chain Security Act was signed into law, which imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new federal legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Furthermore, political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental change. Initiatives to reduce the federal budget and debt and to reform healthcare coverage are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative healthcare benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability. In March 2010, PPACA was signed into law. PPACA has the potential to substantially change the way healthcare is financed by both governmental and private insurers. Among other cost containment measures, PPACA established: an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents; revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; and extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations. In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our products, or the amounts of reimbursement available for our products. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts. Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Regulation in China

The pharmaceutical industry in China is highly regulated. The primary regulatory authority is the NMPA, including its provincial and local branches. As a developer, manufacturer and supplier of drugs, we are subject to regulation and oversight by the NMPA and its provincial and local branches. The Drug Administration Law of China provides the basic legal framework for the administration of the production and sale of pharmaceuticals in China and covers the manufacturing, distributing, packaging, pricing and advertising of pharmaceutical products. Its implementing regulations set forth detailed rules with respect to the administration of pharmaceuticals in China. In addition, we are, and we will be, subject to other Chinese laws and regulations that are applicable to business operators, manufacturers and distributors in general.

Pharmaceutical Clinical Development

A new drug must be approved by the NMPA before it can be manufactured and marketed for sale. To obtain NMPA approval, the applicant must conduct clinical trials, which must be approved by the NMPA and are subject to the NMPA's supervision and inspection. There are four phases of clinical trials. Application for registration of new drugs requires completion of Phase 1, 2 and 3 of clinical trials, similar to the U.S. In addition, the NMPA may require the conduct of Phase 4 studies as a condition to approval.

Phase 4 studies are post-marketing studies to assess the therapeutic effectiveness of and adverse reactions to the new drug, including an evaluation of the benefits and risks, when used among the general population or specific groups, with findings used to inform adjustments to dosage, among other things.

NDA and Approval to Market

China requires approval of the NDA as well as the manufacturing facility before a drug can be marketed in China. Approval and oversight are performed at national and provincial levels of the NMPA, involve multiple agencies and consist of various stages of approval.

Under the applicable drug registration regulations, drug registration applications are divided into three different types, namely Domestic NDA, Domestic Generic Drug Application, and Imported Drug Application. Drugs fall into one of three categories, namely chemical medicine, biological product or traditional Chinese or natural medicine.

Our roxadustat NDA for treatment of CKD anemia was submitted by FibroGen Beijing as a domestic entity under the Domestic Class 1 designation, which refers to a new drug which has never been marketed in any country.

Our NDA package in China contained information similar to what is necessary for a U.S. NDA, including preclinical data, clinical data, technical data on API and drug product, and related stability data.

The NDA package was found acceptable to the NMPA, and FibroGen Beijing was granted a New Drug License confirming the drug as suitable for marketing in December 2018. In addition, FibroGen Beijing was granted a Manufacturing License which lists the Drug Approval Code as well as the name and address of the Manufacturing License holder.

Shortly before NDA approval, FibroGen Beijing conducted a three-batch validation campaign, one of which was observed onsite by the NMPA. Following the successful completion of the validation campaign and associated inspection, FibroGen Beijing was granted a cGMP certification for the commercial production of roxadustat at our Beijing manufacturing facility. We are using our FibroGen Beijing manufacturing facility for commercial supply of drug product. Our Cangzhou manufacturing facility has been fully qualified and licensed for manufacture of roxadustat API for the China market, and we will continue to use this facility for commercial supply. We may also qualify a third party manufacturer to produce commercial API under the Marketing Authorization Holder System program.

Pricing, Reimbursement, Hospital Listing, and Tendering

Please see the discussion above in the section "Roxadustat for the Treatment of Anemia in Chronic Kidney Disease in China."

Foreign Regulation Outside of China

We have received marketing authorization for roxadustat in Japan for anemia of CKD in dialysis patients, and in China for dialysis and non-dialysis patients. Astellas has submitted a supplemental NDA for non-dialysis patients in Japan and intends on submitting an MAA for Europe in the first half of 2020. Our partners also intend to submit for marketing authorization in other countries and we may file for marketing authorization for pamrevlumab or roxadustat in other indications and in other countries in the future. In order to market any product outside of the U.S., we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, manufacturing, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the U.S. apply similarly in the context of other countries we are seeking approval in, including Europe and China, the approval process varies between countries and jurisdictions and can involve different amounts of product testing and additional administrative review periods. For example, in Europe and in China, a sponsor must submit a clinical trial application ("CTA"), much like an IND prior to the commencement of human clinical trials. A CTA must be submitted to each national health authority and an independent ethics committee.

For other countries outside of the Europe, such as China and the countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary from country to country. The time required to obtain approval in other countries and jurisdictions might differ from or be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory approval process in other countries.

Regulatory Exclusivity for Approved Products

U.S. Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The patent term restoration period is generally one-half the time between the effective date of an initial IND and the submission date of an NDA or BLA, plus the time between the submission date of the NDA or BLA and the approval of that product candidate application. Patent term restoration cannot, however, extend the remaining term of a patent beyond a total of 14 years from the product's approval date. In addition, only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for any patent term extension or restoration. In the future, we expect to apply for restoration of patent term for patents relating to each of our product candidates in order to add patent life beyond the current expiration date of such patents, depending on the length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications of companies seeking to reference another company's NDA or BLA. The Hatch-Waxman Act provides a 5-year period of exclusivity to any approved NDA for a product containing a NCE never previously approved by FDA either alone or in combination with another active moiety. No application or abbreviated NDA directed to the same NCE may be submitted during the 5-year exclusivity period, except that such applications may be submitted after four years if they contain a certification of patent invalidity or non-infringement of the patents listed with the FDA by the innovator NDA.

Biologic Price Competition and Innovation Act

The Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory approval pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on similarity to an existing branded product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator BLA holder. The BPCIA is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and interpretation are subject to uncertainty.

Orphan Drug Act

Pamrevlumab has received orphan drug designation in IPF, locally advanced unresectable pancreatic cancer, and DMD in the U.S. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects more than 200,000 individuals in the U.S. there is no reasonable expectation that the cost of developing and making a drug product available in the U.S. for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity in any indication.

The EMA has granted Orphan Medicinal Product Designation to pamrevlumab for the treatment of DMD. Orphan Medicinal Product Designation status in the Europe has similar but not identical benefits in that jurisdiction.

Products receiving orphan designation in the Europe can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation; for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; the initial applicant consents to a second orphan medicinal product application; or the initial applicant cannot supply enough orphan medicinal product. An orphan product can also obtain an additional two years of market exclusivity in the Europe for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

Foreign Country Data Exclusivity

The Europe also provides opportunities for additional market exclusivity. For example, in the Europe, upon receiving marketing authorization, an NCE generally receives eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in the Europe from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity.

In China, there is also an opportunity for data exclusivity for a period of six years for data included in an NDA applicable to a NCE. According to the Provisions for Drug Registration, the Chinese government protects undisclosed data from drug studies and prevents the approval of an application made by another company that uses the undisclosed data for the approved drug. In addition, if an approved drug manufactured in China qualifies as an innovative drug, such as Domestic Class 1, and the NMPA determines that it is appropriate to protect public health with respect to the safety and efficacy of the approved drug, the NMPA may elect to monitor such drug for up to five years. During this post-marketing observation period, the NMPA will not grant approval to another company to produce, change dosage form of or import the drug while the innovative drug is under observation. The approved manufacturer is required to provide an annual report to the regulatory department of the province, autonomous region or municipality directly under the central government where it is located. Each of the data exclusivity period and the observation period runs from the date of approval for production of the NCE or innovative drug, as the case may be.

INTELLECTUAL PROPERTY

Our success depends in part upon our ability to obtain and maintain patent and other intellectual property protection for our product candidates including compositions-of-matter, dosages, and formulations, manufacturing methods, and novel applications, uses and technological innovations related to our product candidates and core technologies. We also rely on trade secrets, know-how and continuing technological innovation to further develop and maintain our competitive position.

Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technologies, inventions and any improvements that we consider important to the development and implementation of our business and strategy. Our ability to maintain and solidify our proprietary position for our products and technologies will depend, in part, on our success in obtaining and enforcing valid patent claims. Additionally, we may benefit from a variety of regulatory frameworks in the U.S., Europe, China, and other territories that provide periods of non-patent-based exclusivity for qualifying drug products. *Refer to "Government Regulation - Regulatory Exclusivity for Approved Products."*

We cannot ensure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications that may be filed by us in the future, nor can we ensure that any of our existing or subsequently granted patents will be useful in protecting our drug candidates, technological innovations, and processes. Additionally, any existing or subsequently granted patents may be challenged, invalidated, circumvented or infringed. We cannot guarantee that our intellectual property rights or proprietary position will be sufficient to permit us to take advantage of current market trends or otherwise to provide or protect competitive advantages. Furthermore, our competitors may be able to independently develop and commercialize similar products, or may be able to duplicate our technologies, business model, or strategy, without infringing our patents or otherwise using our intellectual property.

Our extensive worldwide patent portfolio includes multiple granted and pending patent applications relating to roxadustat and pamrevlumab. Currently granted patents relating to composition-of-matter for roxadustat and for pamrevlumab are expected, for each product candidate, to expire in 2024 or 2025, in each case exclusive of any patent term extension that may be available. U.S. and foreign patents relating to crystalline forms of roxadustat are expected to expire in 2033, exclusive of any extension. Additional patents and patent applications relating to manufacturing processes, formulations, and various therapeutic uses, including treatment of specific indications and improvement of clinical parameters, provide further protection for product candidates.

The protection afforded by any particular patent depends upon many factors, including the type of patent, scope of coverage encompassed by the granted claims, availability of extensions of patent term, availability of legal remedies in the particular territory in which the patent is granted, and validity and enforceability of the patent. Changes in either patent laws or in the interpretation of patent laws in the U.S. and other countries could diminish our ability to protect our inventions and to enforce our intellectual property rights. Accordingly, we cannot predict with certainty the enforceability of any granted patent claims or of any claims that may be granted from our patent applications.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our products and core technologies will depend on our success in obtaining effective claims and enforcing those claims once granted. We have been in the past and are currently involved in various administrative proceedings with respect to our patents and patent applications and may, as a result of our extensive portfolio, be involved in such proceedings in the future. Additionally, in the future, we may claim that a third party infringes our intellectual property or a third party may claim that we infringe its intellectual property. In any of the administrative proceedings or in litigation, we may incur significant expenses, damages, attorneys' fees, costs of proceedings and experts' fees, and management and employees may be required to spend significant time in connection with these actions.

Because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that any patent related to our product candidates may expire before any of our product candidates can be commercialized, or may remain in force for only a short period of time following commercialization, thereby reducing the advantage afforded by any such patent.

The patent positions for our most advanced programs are summarized below.

Roxadustat Patent Portfolio

Our roxadustat patent portfolio includes multiple granted U.S. patents offering protection for roxadustat, including protection for roxadustat composition-of-matter, for pharmaceutical compositions containing roxadustat, and for methods for treating anemia using roxadustat or its analogs. Exclusive of any patent term extension, the granted U.S. patents relating to the composition-of-matter of roxadustat are due to expire in 2024 or 2025, and granted foreign patents are due to expire in 2024. U.S. and foreign patents relating to crystalline forms of roxadustat are due to expire in 2033.

Oppositions were filed against our European Patent No. 2872488 (the "'488 Patent"), which claims a crystalline form of roxadustat. Final resolution of the opposition proceedings will take time, and we cannot be assured of the breadth of the claims that will remain in the '488 Patent or that the patent will not be revoked in its entirety.

We believe that, if roxadustat is approved, a full five-year patent term extension under the Hatch-Waxman act will be available for a granted U.S. patent relating to roxadustat, which extension would expire in 2029 or 2030, depending on the patent extended. *Refer to "Government Regulation - Regulatory Exclusivity for Approved Products - U.S. Patent Term Restoration."*

We also hold various U.S. and foreign granted patents and pending patent applications directed to manufacturing processes, formulations, and methods for use of roxadustat.

Roxadustat China Patent Portfolio

Our roxadustat China patent portfolio includes granted patents covering roxadustat composition-of-matter, pharmaceutical compositions, methods of use, and manufacturing processes for roxadustat, as well as medicaments containing roxadustat for treating anemia and other conditions. Patents relating to roxadustat composition-of-matter and crystalline forms are due to expire in 2024 and 2033, respectively.

We believe that roxadustat, as a new chemical entity, would be eligible for six years of data exclusivity in China. Furthermore, upon approval as a new drug, roxadustat may receive up to five years of market exclusivity under a NMPA-imposed new drug monitoring period. Refer to "Government Regulation - Regulatory Exclusivity for Approved Products - Foreign Country Data Exclusivity."

HIF Anemia-Related Technologies Patent Portfolio

We also have an extensive worldwide patent portfolio providing broad protection for proprietary technologies relating to the treatment of anemia and associated conditions. This portfolio currently contains granted patents and pending patent applications providing exclusivity for use of compounds falling within various and overlapping classes of HIF-PH inhibitors to achieve various therapeutic effects.

This portfolio reflects a series of discoveries we made from the initial days of our HIF program through the present time. Our research efforts have resulted in progressive innovation, and the corresponding patents and patent applications reflect the success of our HIF program. Such discoveries include the ability of HIF-PH inhibitors:

- To induce endogenous EPO in CKD patients with anemia.
- To increase efficacy of EPO signaling.
- To enhance EPO responsiveness of the bone marrow, for example, by increasing EPO receptor expression.
- To overcome the suppressive and inhibitory effects of inflammatory cytokines, such as members of the interleukin-1 and IL-6 cytokine families, on EPO production and responsiveness.
- To increase effective metabolism of iron.
- To increase iron absorption and bioavailability, as measured using clinical parameters such as percent TSAT%.
- To overcome iron deficiency through effects on iron regulatory factors such as ferroportin and hepcidin.
- · To provide coordinated erythropoiesis resulting in increased CHr and increased mean corpuscular volume.
- To improve kidney function.

The table below sets forth representative granted U.S. patents relating to these and other inventions, including the projected expiration dates of these patents.

PATENT NO.	тпе	DUE TO EXPIRE
6,855,510	Pharmaceuticals and Methods for Treating Hypoxia and Screening Methods Therefor	July 2022
8,466,172	Stabilization of Hypoxia Inducible Factor (HIF) Alpha	December 2022
8,629,131	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,604,012	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,609,646	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,604,013	Enhanced Erythropoiesis and Iron Metabolism	June 2024
8,614,204	Enhanced Erythropoiesis and Iron Metabolism	June 2026
7,713,986	Compounds and Methods for Treatment of Chemotherapy-Induced Anemia	June 2026
8,318,703	Methods for Improving Kidney Function	February 2027

In addition to the U.S. patents listed above, our HIF anemia-related technologies portfolio includes corresponding foreign patents granted and patent applications pending in various territories worldwide.

Akebia and others have filed oppositions against certain European patents within our HIF anemia-related technologies patent portfolio. In three of these proceedings, for FibroGen European Patent Nos. 1463823, 1633333, and 2322155, the European Patent Office has handed down decisions unfavorable to FibroGen. In the fourth of these proceedings, the European Patent Office issued a decision favorable to FibroGen, maintaining FibroGen European Patent No. 2322153 in amended form. All of these decisions are currently under appeal, and these four patents are valid and enforceable pending resolution of the appeals. The ultimate outcomes of such proceedings remain uncertain, and ultimate resolution of such may take considerable time.

In addition, Akebia has filed oppositions against FibroGen European Patent Nos. 2289531 and 2298301. Akebia and GSK have also initiated invalidation actions in the United Kingdom against the United Kingdom counterparts of each of these European patents, and GSK has filed for a declaration of non-infringement of certain United Kingdom patents (corresponding to FibroGen European Patent Nos. 2322153 and 2322155) with respect to its daprodustat product. Akebia is also pursuing invalidation actions against corresponding patents in Canada and in Japan, and invalidation actions against corresponding patents in the United Kingdom have been initiated by GSK and by Akebia, although FibroGen has reached an agreement with GSK that will lead to dismissal of the UK court actions and the proceedings filed by GSK against the patents in the EPO. Astellas' proceedings brought against GSK on a *quia timet* basis have also been dismissed as a result of the settlement agreement. While we believe the ultimate outcome of all proceedings will be that these FibroGen patents will be upheld in relevant part, we note that narrowing or even revocation of any of these patents would not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia.

Pamrevlumab Patent Portfolio

Our pamrevlumab patent portfolio includes U.S. patents providing composition-of-matter protection for pamrevlumab and related antibodies, and for methods of using such in the treatment of fibroproliferative disorders, including IPF, liver fibrosis, and pancreatic cancer. Exclusive of any patent term extension, U.S. patents relating to pamrevlumab composition-of-matter are due to expire in 2024 or 2025. Corresponding foreign patents are due to expire, exclusive of any patent term extension, in 2024.

We believe that, if pamrevlumab is approved, a full five-year patent term extension under the Hatch-Waxman act will be available for a granted patent relating to pamrevlumab, which extension would expire in 2029 or 2030, depending on the patent extended. In addition, we believe that pamrevlumab, if approved under a BLA, should qualify for the 12-year period of exclusivity currently permitted by the BPCIA. Refer to "Government Regulation - Regulatory Exclusivity for Approved Products."

We also hold additional granted U.S. and foreign patents and pending patent applications directed to the use of pamrevlumab to treat IPF, DMD, pancreatic cancer, liver fibrosis, and other disorders.

Trade Secrets and Know-How

In addition to patents, we rely upon proprietary trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality and other terms in agreements with our commercial partners, collaboration partners, consultants and employees. Such agreements are designed to protect our proprietary information, and may also grant us ownership of technologies that are developed through a relationship with a third party, such as through invention assignment provisions. Agreements may expire and we could lose the benefit of confidentiality, or our agreements may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

To the extent that our commercial partners, collaboration partners, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

In-Licenses

Dana-Farber Cancer Institute

Effective March 2006, we entered into a license agreement with the Dana-Farber Cancer Institute ("DFCI"), under which we obtained an exclusive license to certain patent applications, patents and biological materials for all uses. The patent rights relate to inhibition of prolyl hydroxylation of the alpha subunit of hypoxia-inducible factor (HIFα), and include granted U.S. and foreign patents due to expire in 2022, exclusive of possible patent term extension. The licensed patents relate to use of HIF-PH inhibitors such as roxadustat.

Under the DFCI agreement, we are obligated to pay DFCI for past and ongoing patent prosecution expenses for the licensed patents. We are also obligated to pay DFCI annual maintenance fees, development milestone payments of up to \$425,000, sales milestone payments of up to \$3 million, and a sub-single-digit royalty on net sales by us or our affiliates or sublicensees of products that are covered by the licensed patents or incorporate the licensed biological materials. In addition, each sublicense we grant is subject to a one-time fixed amount payment to DFCI.

Unless earlier terminated, the agreement will continue in effect, on a country-by-country basis, until the expiration of all licensed patents in a country or, if there is no patent covering a licensed product incorporating the licensed biological materials, until 20 years after the effective date of the agreement. DFCI may terminate the agreement for our uncured material breach, if we cease to carry on our business and development activities with respect to all licensed products, if we fail to comply with our insurance obligations, or if we are convicted of a felony related to the manufacture, use, sale or importation of licensed products. We may terminate the agreement at any time on prior written notice to DFCI.

University of Miami

In May 1997, we entered into a license agreement with the University of Miami (the "University"), amended in July 1999, under which we obtained an exclusive, worldwide license to certain patent applications and patents for all uses. The current patent rights consist of a U.S. patent that relates to antibodies that specifically bind to biologically active fragments of CTGF, and is due to expire in 2022, exclusive of any patent term extension or adjustment that may be available. The licensed patent relates to pamrevlumab and related products.

Under the University agreement, we are obligated to pay for all ongoing patent expenses for the licensed patent. We were also obligated to pay an upfront licensing fee of \$21,500, all of which has been paid, and development milestone payments of up to \$450,000, of which \$150,000 has been paid, as well as an additional milestone payment, in the low hundreds of thousands of dollars, for each new indication for which we obtain approval for a licensed product, and a single digit royalty, subject to certain reductions, on net sales of licensed products by us or our affiliates or sublicensees.

Unless earlier terminated, the agreement will continue in effect, on a country-by-country basis, until the expiration of all licensed patents in a country. The University may terminate the agreement for our uncured material breach or bankruptcy. We may terminate the agreement for the University's uncured material breach or at any time on prior written notice to the University.

Bristol-Myers Squibb Company (Medarex, Inc.)

Effective July 9, 1998 and as amended on June 30, 2001 and January 28, 2002, we entered into a research and commercialization agreement with Medarex, Inc. and its wholly-owned subsidiary GenPharm International, Inc. (now, collectively, part of Bristol-Myers Squibb Company ("Medarex")) to develop fully human monoclonal antibodies for potential anti-fibrotic therapies. Under the agreement, Medarex was responsible for using its proprietary immunizable transgenic mice ("HuMAb-Mouse technology") during a specified research period ("the Research Period"), to produce fully human antibodies against our proprietary antigen targets, including CTGF, for our exclusive use.

The agreement granted us an option to obtain an exclusive worldwide, royalty-bearing, commercial license to develop antibodies derived from Medarex's HuMAb-Mouse technology, for use in the development and commercialization of diagnostic and therapeutic products. In December 2002, we exercised that option with respect to twelve antibodies inclusive of the antibody from which pamrevlumab is derived. We granted back to Medarex an exclusive, worldwide, royalty-free, perpetual, irrevocable license, with the right to sublicense, to certain inventions created during the parties' research collaboration, with such license limited to use by Medarex outside the scope of our licensed antibodies.

As a result of the exercise of our option to obtain the commercial license, Medarex is precluded from (i) knowingly using any technology involving immunizable transgenic mice containing unrearranged human immunoglobulin genes with any of our antigen targets that were the subject of the agreement, (ii) granting to a third party a commercial license that covers such antigen targets or those antibodies derived by Medarex during the Research Period, and (iii) using any antibodies derived by Medarex during the Research Period, except as permitted under the agreement for our benefit or to prosecute patent applications in accordance with the agreement.

Medarex retained ownership of the patent rights relating to certain mice, mice materials, antibodies and hybridoma cell lines used by Medarex in connection with its activities under the agreement, and Medarex also owns certain claims in patents covering inventions that arise during the Research Period, which claims are directed to (i) compositions of matter (e.g., an antibody) except formulations of antibodies for therapeutic or diagnostic use, or (ii) methods of production. We own the patent rights to any inventions that arise during the Research Period that relate to antigens, as well as claims in patents covering inventions directed to (a) methods of use of an antibody, or (b) formulations of antibodies for therapeutic or diagnostic use. Upon exercise of our option to obtain the commercial license, we obtained the sole right but not obligation to control prosecution of patents relating solely to the licensed antibodies or products. Medarex has back-up patent prosecution rights in the event we decline to further prosecute or maintain such patents.

In addition to research support payments by us to Medarex during the Research Period, and an upfront commercial license fee in the form of 181,819 shares of FibroGen Series D Convertible Preferred Stock paid upon exercise of our option, we committed development-related milestone payments of up to \$11 million per therapeutic product containing a licensed antibody, and we have paid a \$1 million development-related milestone, in the form of 133,333 shares of FibroGen Series G Convertible Preferred Stock, and a cash payment of \$2 million, for pamrevlumab to date. At our election, the remaining milestone payments may be paid in common stock of FibroGen, Inc., or cash.

With respect to our sales and sales by our affiliates, the agreement also requires us to pay Medarex low single-digit royalties for licensed therapeutic products and low double-digit royalties plus certain capped sales-based bonus royalties for licensed diagnostic products. With respect to sales of licensed products by a sublicensee, we may elect to pay the foregoing royalties based on our sublicensee's sales, or a percentage (in the high-teens) of all payments received by us from such sublicensee. We are also required to reimburse Medarex any pass-through royalties, if any, payable under Medarex's upstream license agreements with Medical Research Council and DNX. Royalties payable by us under the agreement are on a licensed product-by-licensed product and country-by-country basis and subject to reductions in specified circumstances, and royalties are payable for a period until either expiration of patents covering the applicable licensed product or a specified number of years following the first commercial sale of such product in the applicable country.

Unless earlier terminated, the agreement will continue in effect for as long as there are royalty payment obligations by us or our sublicensees. Either party may terminate the agreement for certain material breaches by the other party, or for bankruptcy, insolvency or similar circumstances. In addition, we may also terminate the agreement for convenience upon written notice.

Third Party Filings

Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing products. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in granted patents that use of our product candidates or proprietary technologies may infringe.

If a third party claims that we infringe its intellectual property rights, we may face a number of issues, including but not limited to, litigation expenses, substantial damages, attorney fees, injunction, royalty payments, cross-licensing of our patents, redesign of our products, or processes and related fees and costs.

We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our products, product candidates, and/or proprietary technologies infringe their intellectual property rights. If one of these patents were to be found to cover our products, product candidates, proprietary technologies, or their uses, we could be required to pay damages and could be restricted from commercializing our products, product candidates or using our proprietary technologies unless we obtain a license to the patent. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the patent holder might obtain a preliminary injunction or other equitable right, which could prohibit us from making, using or selling our products, technologies, or methods.

EMPLOYEES

As of January 31, 2020, we had 531 full-time employees, 136 of whom held Ph.D. or M.D. degrees, 279 of whom were engaged in research and development and 252 of whom were engaged in manufacturing, sales and marketing, business development, finance, information systems, facilities, human resources or administrative support. None of our U.S. employees are represented by a labor union. The employees of FibroGen Beijing are represented by a labor union under the China Labor Union Law. None of our employees have entered into a collective agreement with us. We consider our employee relations to be good.

FACILITIES

Our corporate and research and development operations are located in San Francisco, California, where we lease approximately 234,000 square feet of office and laboratory space with approximately 35,000 square feet subleased. The lease for our San Francisco headquarters expires in 2023. We also lease approximately 67,000 square feet of office and manufacturing space in Beijing, China. Our lease in China expires in 2021. We have constructed a commercial manufacturing facility of approximately 5,500 square meters in Cangzhou, China, on approximately 33,000 square meters of land. Our right to use such land expires in 2068. We believe our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

FINANCIAL INFORMATION

Information regarding our revenues, net loss and total assets is contained in our consolidated financial statements under Item 8 of this Annual Report, which information is incorporated by reference here. For the specifics of our segment and geographic revenue, refer to Note 14 to our consolidated financial statements.

Research and development expenses for fiscal years ended December 31, 2019, 2018 and 2017 were \$209.3 million, \$235.8 million, and \$196.5 million, respectively. We expect our research and development expenses to continue to increase in the future as we advance our product candidates through clinical trials and expand our product candidate portfolio.

Our revenue to date has been generated primarily from our collaboration agreements with Astellas and AstraZeneca for the development and commercialization of roxadustat. For fiscal years ended December 31, 2019, 2018 and 2017, substantially all of our revenue was related to our collaboration agreements.

AVAILABLE INFORMATION

Our internet website address is www.fibrogen.com. In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. Our website and information included in or linked to our website are not part of this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission ("SEC"). Additionally the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

CORPORATE INFORMATION

We were incorporated in 1993 in Delaware. Our headquarters are located at 409 Illinois Street, San Francisco, California 94158 and our telephone number is (415) 978-1200. Our website address is www.FibroGen.com. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated into, this Annual Report.

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Our subsidiaries consist of the following: 1) FibroGen Europe Oy ("FibroGen Europe"), a majority owned entity incorporated in Finland in 1996; 2) Skin Sciences, Inc., a majority owned entity incorporated in the State of Delaware in 1995; 3) FibroGen International (Cayman) Limited, a majority owned entity incorporated in the Cayman Islands in 2011; 4) FibroGen China Anemia Holdings Ltd., a majority owned entity incorporated in the Cayman Islands in 2012; 5) FibroGen International (Hong Kong) Limited, a majority owned entity incorporated in Hong Kong in 2011; and 6) FibroGen (China) Medical Technology Development Co., Ltd., a majority owned entity incorporated in China in 2011.

"FibroGen," the FibroGen logo and other trademarks or service marks of FibroGen, Inc. appearing in this Annual Report are the property of FibroGen, Inc. This Annual Report contains additional trade names, trademarks and service marks of others, which are the property of their respective owners. We do not intend our use of display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below in addition to the other information included or incorporated by reference in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Risks Related to Our Financial Condition and History of Operating Losses

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or sustain profitability. We may require additional financings in order to fund our operations.

We are a biopharmaceutical company with two lead product candidates in clinical development, roxadustat in anemia in chronic kidney disease ("CKD"), myelodysplastic syndromes ("MDS"), and chemotherapy-induced anemia, and pamrevlumab in idiopathic pulmonary fibrosis ("IPF"), pancreatic cancer, and Duchenne muscular dystrophy ("DMD"). Most of our revenue generated to date has been based on our collaboration agreements and we have limited commercial drug product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss for the year ended December 31, 2019, 2018 and 2017 were \$77.0 million, \$86.4 million and \$120.9 million, respectively. As of December 31, 2019, we had an accumulated deficit of \$784.7 million. As of December 31, 2019, we had capital resources consisting of cash, cash equivalents and short-term investments of \$533.8 million plus \$61.1 million of long-term investments classified as available for sale securities. Despite contractual development and cost coverage commitments from our collaboration partners, AstraZeneca AB ("AstraZeneca") and Astellas Pharma Inc. ("Astellas"), and the potential to receive milestone and other payments from these partners, and despite commercialization efforts in the People's Republic of China ("China") and Japan for roxadustat for the treatment of anemia caused by CKD, we anticipate we will continue to incur losses on an annual basis for the foreseeable future. If we do not successfully develop and continue to obtain regulatory approval for our existing or any future product candidates and effectively manufacture, market and sell the product candidates that are approved, we may never achieve or sustain profitability on a quarterly or annual basis. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

We believe that we will continue to expend substantial resources for the foreseeable future as we continue late-stage clinical development of roxadustat, grow our operations in China, expand our clinical development efforts on pamrevlumab, continue to seek regulatory approval, launch commercialization of our product candidates, and pursue additional indications. These expenditures will include costs associated with research and development, conducting preclinical trials and clinical trials, obtaining regulatory approvals in various jurisdictions, and manufacturing and supplying products and product candidates for ourselves and our partners. The outcome of any clinical trial and/or regulatory approval process is highly uncertain and we are unable to fully estimate the actual costs necessary to successfully complete the development and regulatory approval process for our compounds in development and any future product candidates. We believe that the net proceeds from our 2017 public offerings, our existing cash and cash equivalents, short-term and long-term investments and accounts receivable, and expected third-party collaboration revenues will allow us to fund our operating plans through at least the next 12 months. Our operating plans or third-party collaborations may change as a result of many factors, including the success of our development and commercialization efforts, operations costs (including manufacturing and regulatory), competition, and other factors that may not currently be known to us, and we therefore may need to seek additional funds sooner than planned, through offerings of public or private securities, debt financings or other sources, such as royalty monetization or other structured financings. Such financings may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. We may also seek additional capital due to favorable market conditions or strategic considerations even if we currently believe

Additional funds may not be available when we require them, or on terms that are acceptable to us. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations or activities that may be necessary to commercialize our product candidates.

Most of our recent revenue has been earned from collaboration partners for our product candidates under development.

If either or both of our Astellas and AstraZeneca collaborations were to be terminated, we could require significant additional capital in order to proceed with development and commercialization of our product candidates, including with respect to our commercialization of roxadustat for the treatment of anemia caused by CKD, or we may require additional partnering in order to help fund such development and commercialization. If adequate funds or partners are not available to us on a timely basis or on favorable terms, we may be required to delay, limit, reduce or terminate our development or commercialization efforts or other operations.

Risks Related to the Development and Commercialization of Our Product Candidates

We are substantially dependent on the success of our lead product, roxadustat, and our second compound in development, pamrevlumab.

To date, we have invested a substantial portion of our efforts and financial resources in the research and development of roxadustat and pamrevlumab. While we have received approval of our New Drug Applications ("NDA") for roxadustat in China for CKD anemia for patients on dialysis and not on dialysis, and for roxadustat in Japan for CKD anemia in dialysis patients, we will need to make substantial additional investments in both the development and commercialization of roxadustat worldwide and in various indications. Our near-term prospects, including maintaining our existing collaborations with Astellas and AstraZeneca, will depend heavily on successful development and commercialization of roxadustat, including obtaining regulatory approvals for the commercialization of roxadustat for anemia associated with CKD.

Our other lead product candidate, pamrevlumab, is currently in clinical development for IPF, pancreatic cancer and DMD. Pamrevlumab requires substantial further development and investment and we do not have a collaboration partner for support of this compound. In addition, pamrevlumab is a monoclonal antibody, which may require greater financial resources than for our small molecule, roxadustat.

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, many of which are beyond our control, and we may be unable to complete the development or commercialization of roxadustat or pamrevlumab.

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, including the following:

- the timely initiation and completion of our clinical trials;
- our ability to demonstrate the safety and efficacy of our product candidates to the satisfaction of the relevant regulatory authorities;
- the ultimate approval criteria (which may include non-inferiority margins and statistical analyses methods), indications, patient populations, and ultimate benefit-risk analysis used by regulatory authorities in their approval processes;
- whether we are required by the United States ("U.S.") Food and Drug Administration ("FDA") or other regulatory authorities to conduct additional clinical trials, and the scope and nature of such clinical trials, prior to approval to market our products;
- the clinical indications for which the product is approved and the labeling required by regulatory authorities for use with the product, including any warnings that may be required in the labeling;
- the receipt or timely receipt of marketing approvals from the FDA and foreign regulatory authorities, including pricing and reimbursement determinations;
- the ability to successfully commercialize, market, sell and distribute our product candidates, if approved, for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;
- whether we or our partners are able to recruit and retain adequate numbers of effective sales and marketing personnel for the sale of our products;
- whether we will maintain sufficient funding to cover the costs and expenses associated with creating and sustaining a capable sales and marketing organization and related commercial infrastructure;
- whether we can compete successfully as a new entrant in the treatment of anemia caused by CKD;
- our ability and the ability of our third-party manufacturing partners to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability;

- our success in educating health care providers, patients and the healthcare community about the benefits, risks, administration and use of our product candidates, if approved;
- acceptance of our product candidates, if approved, as safe and effective by patients and the healthcare community;
- the success of efforts to enter into relationships with large dialysis organizations involving the administration of roxadustat to dialysis patients;
- the achievement and maintenance of compliance with all regulatory requirements applicable to us and our product candidates;
- the maintenance of an acceptable safety profile of our products following any approval;
- the availability, perceived advantages, relative cost, relative safety, and relative efficacy of alternative and competitive treatments;
- the restrictions on the use of our products together with other medications, if any;
- our ability to negotiate, obtain and sustain an adequate level of pricing or reimbursement for our products by third-party payors;
- the availability of adequate coverage and reimbursement or pricing by third-party payors and government authorities;
- our ability to enforce successfully our intellectual property rights for our product candidates and against the products of potential competitors:
- our ability to avoid or succeed in third-party patent interference or patent infringement claims; and
- sufficient stability data for launch and market supply.

Many of these factors are beyond our control. Successful commercialization of our products will require significant resources and time, and there is a risk that we may not successfully commercialize them. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our products and generate revenues, which would deprive us from additional working capital and would materially harm our ability to achieve profitability through the sale of or royalties from our product candidates.

As a company, we have limited commercialization experience, and the time and resources to develop such experience are significant. If we fail to achieve and sustain commercial success for roxadustat, either directly or with our collaboration partners, our business would be harmed.

We do not have a sales or marketing infrastructure and have no experience in the sales, marketing or distribution of pharmaceutical products in any country. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales and marketing capabilities or make and maintain our existing arrangements with third parties to perform these services at a level sufficient to support our commercialization efforts.

To the extent that we would undertake sales and marketing of any of our products directly, there are risks involved with establishing our own sales, marketing and distribution capabilities. Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to effectively manage geographically dispersed sales and marketing teams;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

With respect to roxadustat, we are dependent on the commercialization capabilities of our collaboration partners, AstraZeneca and Astellas. If either such partner were to terminate its agreement with us, we would have to commercialize on our own or with another third party. We will have limited or little control over the commercialization efforts of such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products, if any, effectively. If they are not successful in commercializing our product candidates, our business and financial condition would suffer.

Commercializing roxadustat requires us to establish commercialization systems, including but not limited to, medical affairs, sales, pharmacovigilance, supply-chain, and distribution capabilities to perform our portion of the collaborative efforts. These efforts require resources and time. If we, along with Astellas and AstraZeneca, are not successful in setting our marketing, pricing and reimbursement strategy, facilitating adoption by hospitals, recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing roxadustat, which would adversely affect our business and financial condition.

Although regulatory approval has been obtained for roxadustat in China and Japan, we may be unable to obtain regulatory approval for our product candidates in other countries, or such approval may be delayed or limited, due to a number of factors, many of which are beyond our control.

The clinical trials and the manufacturing of our product candidates are and will continue to be, and the marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to develop and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical trials and clinical trials that the product candidate is safe and effective for use in each indication for which approval is sought. The regulatory review and approval process is expensive and requires substantial resources and time, and in general very few product candidates that enter development receive regulatory approval. In addition, our collaboration partners for roxadustat have final control over development decisions in their respective territories and they may make decisions with respect to development or regulatory authorities that delay or limit the potential approval of roxadustat, or increase the cost of development or commercialization. Accordingly, we may be unable to successfully develop or commercialize roxadustat or pamrevlumab or any of our other product candidates in one or more indications and jurisdictions.

Moreover, for any Phase 3 clinical trial to support an NDA submission for approval, the FDA and foreign regulatory authorities require compliance with regulations and standards (including good clinical practices ("GCP") requirements for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials) to ensure that (1) the data and results from trials are credible and accurate; and (2) that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we as the sponsor remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable. Accordingly, the FDA or other regulatory authorities may require us to exclude the use of patient data from these unreliable clinical trials, or perform additional clinical trials before approving our marketing applications. The FDA or other regulatory authorities may even reject our application for approval or refuse to accept our future applications.

Regulatory authorities may take actions or impose requirements that delay, limit or deny approval of our product candidates for many reasons, including, among others:

- our failure to adequately demonstrate to the satisfaction of regulatory authorities that roxadustat is safe and effective in treating anemia in CKD or that pamrevlumab is safe and effective in treating IPF, pancreatic cancer or DMD;
- our failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- our failure of clinical trials to meet the level of statistical significance required for approval;
- the determination by regulatory authorities that additional clinical trials are necessary to demonstrate the safety and efficacy of
 roxadustat or pamrevlumab, or that ongoing clinical trials need to be modified in design, size, conduct or implementation;
- our product candidates may exhibit an unacceptable safety signal as they advance through clinical trials, in particular controlled Phase 3 trials;

- the clinical research organizations ("CROs") that conduct clinical trials on our behalf may take actions outside of our control that materially adversely impact our clinical trials;
- we or third-party contractors manufacturing our product candidates may not maintain current good manufacturing practices ("cGMP"), successfully pass inspection or meet other applicable manufacturing regulatory requirements;
- regulatory authorities may not agree with our interpretation of the data from our preclinical trials and clinical trials; or
- collaboration partners may not perform or complete their clinical programs in a timely manner, or at all.

Any of these factors, many of which are beyond our control, could jeopardize our or our collaboration partners' abilities to obtain regulatory approval for our product candidates in one or more indications.

The FDA or other regulatory authorities may require more information (including additional preclinical or clinical data to support approval), which may delay or prevent approval or cause us to abandon the development program altogether. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS (or other regulatory authorities may require the establishment of a similar strategy), that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us.

Preclinical, Phase 1 and Phase 2 clinical trial results may not be indicative of the results that may be obtained in larger, controlled Phase 3 clinical trials required for approval.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical and early clinical trials, which are often highly variable and use small sample sizes, may not be predictive of similar results in humans or in larger, controlled clinical trials, and successful results from clinical trials in one indication may not be replicated in other indications.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may face similar setbacks.

We do not know whether our ongoing or planned clinical trials of roxadustat or pamrevlumab will need to be redesigned based on interim results or if we will be able to achieve sufficient patient enrollment or complete planned clinical trials on schedule.

Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- address any physician or patient safety concerns that arise during the course of the trial;
- obtain required regulatory or institutional review board approval or guidance;
- reach timely agreement on acceptable terms with prospective CROs and clinical trial sites;
- recruit, enroll and retain patients through the completion of the trial;
- maintain clinical sites in compliance with clinical trial protocols;
- initiate or add a sufficient number of clinical trial sites; and
- manufacture sufficient quantities of product candidate for use in clinical trials.

In particular, identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the rate at which we can recruit and enroll patients in testing our product candidates. Patients may be unwilling to participate in clinical trials of our product candidates for a variety of reasons, some of which may be beyond our control, including:

- severity of the disease under investigation;
- availability of alternative treatments;
- size and nature of the patient population;
- eligibility criteria for and design of the study in question;
- perceived risks and benefits of the product candidate under study;
- ongoing clinical trials of competitive agents;

- physicians' and patients' perceptions of the potential advantages of our product candidates being studied in relation to available therapies or other products under development;
- our CRO's and our trial sites' efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients and collect patient data adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials.

In addition, we could encounter delays if a clinical trial is suspended or terminated by us, by the relevant institutional review boards at the sites at which such trials are being conducted, or by the FDA or other regulatory authorities. A suspension or termination of clinical trials may result from any number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or a principal investigator's determination that a serious adverse event could be related to our product candidates. Any delays in completing our clinical trials will increase the costs of the trial, delay the product candidate development and approval process and jeopardize our ability to commence marketing and generate revenues. Any of these occurrences may materially and adversely harm our business and operations and prospects.

Our product candidates may cause or have attributed to them undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our product candidates or that may be identified as related to our product candidates by physician investigators conducting our clinical trials or even competing products in development that utilize a similar mechanism of action or act through a similar biological disease pathway could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. If we determine that there is a likely causal relationship between a serious adverse event and our product candidate, and such safety event is material or significant enough, it may result in:

- our Phase 3 clinical trial development plan becoming longer and more extensive;
- regulatory authorities increasing the data and information required to approve our product candidates and imposing other requirements; and
- our collaboration partners terminating our existing agreements.

The occurrence of any or all of these events may cause the development of our product candidates to be delayed or terminated, which could materially and adversely affect our business and prospects. Refer to "Business - Roxadustat for the Treatment of Anemia in Chronic Kidney Disease" and "Business - Pamrevlumab for the Treatment of Fibrosis and Cancer" for a discussion of the adverse events and serious adverse events that have emerged in clinical trials of roxadustat and pamrevlumab.

Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.

Clinical trials are conducted in representative samples of the potential patient population, which may have significant variability. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, that a more complete safety profile is identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. There have been other products, including erythropoiesis stimulating agents ("ESAs"), for which safety concerns have been uncovered following approval by regulatory authorities. Such safety concerns have led to labeling changes or withdrawal of ESAs products from the market. While our most advanced product candidate is chemically unique from ESAs, it or any of our product candidates may be subject to known or unknown risks. Patients treated with our products, if approved, may experience adverse reactions and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If safety problems occur or are identified after our product candidates reach the market, we may, or regulatory authorities may require us to amend the labeling of our products, recall our products or even withdraw approval for our products.

If we or third-party manufacturers and other service providers on which we rely cannot manufacture sufficient quantities of our product candidates, or at sufficient quality, or perform other services we require, we may experience delays in development, regulatory approval, launch or successful commercialization.

Completion of our clinical trials and commercialization of our product candidates require access to, or development of, facilities to manufacture and manage our product candidates at sufficient yields, quality and at commercial scale. Although we have entered into commercial supply agreements for the manufacture of some of our drug candidates, active pharmaceutical ingredients, intermediates or raw materials, we will need to enter into additional commercial supply agreements, including for backup or second source third-party manufacturers. We may not be able to enter into these agreements with satisfactory terms or on a timely manner.

We have limited experience manufacturing or managing third parties in manufacturing any of our product candidates in the volumes that are expected to be necessary to support large-scale clinical trials and sales. In addition, we have limited experience forecasting supply requirements or coordinating supply chain (including export management) for launch or commercialization, which is a complex process involving our third-party manufacturers and logistics providers, and for roxadustat, our collaboration partners. We may not be able to accurately forecast supplies for commercial launch, or do so in a timely manner and our efforts to establish these manufacturing and supply chain management capabilities may not meet our requirements as to quantities, scale-up, yield, cost, potency or quality in compliance with cGMP, particularly if the marketing authorization or market uptake is more rapid than anticipated.

We have a limited amount of roxadustat and pamrevlumab in storage, limited capacity reserved at our third-party manufacturers, and there are long lead times required to manufacture and scale-up the manufacture of additional supply, as required for both late-stage clinical trials, post-approval trials, and commercial supply. If we are unable to forecast, order or manufacture sufficient quantities of roxadustat or pamrevlumab on a timely basis, it may delay our development, launch or commercialization in some or all indications we are currently pursuing. Any delay or interruption in the supply of our product candidates or products could have a material adverse effect on our business and operations.

Our clinical trials must be conducted with product produced under applicable cGMP regulations. Failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. We, and even an experienced third-party manufacturer, may encounter difficulties in production. Difficulties may include:

- costs and challenges associated with scale-up and attaining sufficient manufacturing yields, in particular for biologic products such as pamrevlumab, which is a monoclonal antibody;
- supply chain issues, including coordination of multiple contractors in our supply chain and securing necessary licenses (such as export licenses);
- the timely availability and shelf life requirements of raw materials and supplies;
- quality control and quality assurance;
- shortages of qualified personnel and capital required to manufacture large quantities of product;
- compliance with regulatory requirements that vary in each country where a product might be sold;
- · capacity or forecasting limitations and scheduling availability in contracted facilities; and
- natural disasters, such as floods, storms, earthquakes, tsunamis, and droughts, or accidents such as fire, that affect facilities, possibly
 limit or postpone production, and increase costs.

The FDA and European Medicines Agency will do their own benefit risk analysis and may reach a different conclusion than we or our partners have internally, and these regulatory authorities may base their approval decision on different analyses, data, and statistical methods than ours.

Even if we believe we have achieved positive clinical results, such as superiority or non-inferiority, in certain endpoints, populations or subpopulations, or using certain statistical methods of analysis, the FDA and European Medicines Agency will each conduct their own benefit-risk analysis and may reach different conclusions, using different statistical methods, different endpoints or definitions thereof, or different patient populations or sub-populations, and regulatory authorities may change their approvability criteria based on their internal analyses and discussions with expert advisors. Regulatory authorities may approve roxadustat for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-approval clinical trials. While we will present to regulatory authorities certain pre-specified and not pre-specified sub-populations and sub-group analyses (for example, incident dialysis), multiple secondary endpoints, and multiple analytical methods (such as long-term follow up analyses), including adjusted and censored data, regulatory authorities may reject these analyses, methods, or even parts of our trial design or certain data from our studies, the rationale for our pre-specified non-inferiority margins or other portions of our statistical analysis plans. In addition, even if we are able to provide positive data with respect to certain analyses, such as incident dialysis, estimated glomerular filtration rate, hepcidin, or quality of life measures, regulatory authorities may not include such claims on any approved labeling for roxadustat, which may limit the commercialization or market opportunity for roxadustat. The failure to obtain regulatory approval, or any label, population or other approval limitations in any jurisdiction, may significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenue.

Even if we are able to obtain regulatory approval of our product candidates, the label we obtain may limit the indicated uses for which our product candidates may be marketed.

With respect to roxadustat, regulatory approvals obtained, could limit the approved indicated uses for which roxadustat may be marketed. For example, our label approved in Japan, includes the following warning: "Serious thromboembolism such as cerebral infarction, myocardial infarction, and pulmonary embolism may occur, possibly resulting in death, during treatment with roxadustat." Additionally, in the U.S., ESAs have been subject to significant safety warnings, including the "Black Box" warnings on their labels. The safety concerns relating to ESAs may result in labeling for roxadustat containing similar warnings even if our Phase 3 clinical trials do not suggest that roxadustat has similar safety issues. Even if the label for roxadustat does not contain all of the warnings contained in the "Black Box" warning for ESAs, the label for roxadustat may contain other warnings or limit the market opportunity or approved indications for roxadustat. These warnings could include warnings against exceeding specified hemoglobin targets and other warnings that derive from the lack of clarity regarding the safety issues associated with ESAs, even if our Phase 3 clinical trials do not themselves raise safety concerns.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.

The development and commercialization of new pharmaceutical products is highly competitive. Our future success depends on our ability to achieve and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to discover, develop and commercialize new products with superior efficacy, convenience, tolerability, and safety. We expect that in many cases, the products that we commercialize will compete with existing, market-leading products of companies that have large, established commercial organizations.

If roxadustat is approved and launched commercially, competing drugs are expected to include ESAs, particularly in those patient segments where ESAs are used. Currently available ESAs include epoetin alfa (EPOGEN ®, marketed by Amgen Inc. in the U.S., Procrit ® and Erypo ®/Eprex ®, marketed by Johnson & Johnson Inc., and Espo ® marketed by Kyowa Hakko Kirin in Japan and China), darbepoetin (Amgen/Kyowa Hakko Kirin's Aranesp ® and NESP ®) and Mircera ® marketed by Hoffmann-La Roche ("Roche") outside of the U.S. and by Vifor Pharma, a Roche licensee, in the U.S. and Puerto Rico, as well as biosimilar versions of these currently marketed ESA products. ESAs have been used in the treatment of anemia in CKD for more than 20 years, serving a significant majority of dialysis-dependent CKD patients. While non-dialysis-dependent CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated, some patients under nephrology care may be receiving ESA therapy. It may be difficult to encourage healthcare providers and patients to switch to roxadustat from products with which they have become familiar.

We may also face competition from potential new anemia therapies currently in clinical development, including in those patient segments not currently addressed by ESAs. Companies that are currently developing HIF-PH inhibitors for anemia in CKD indications include GlaxoSmithKline plc ("GSK"), Bayer Corporation ("Bayer"), Akebia Therapeutics, Inc. ("Akebia"), Japan Tobacco, and Zydus Cadila. Akebia is currently conducting Phase 3 studies in CKD patients on dialysis and not on dialysis, as well as a Phase 2 study evaluating pharmacokinetics and pharmacodynamics in dialysis-dependent patients with three-times weekly versus once-a-day dosing. Akebia expects to complete these studies by August 2020. In Japan, Mitsubishi Tanabe Pharmaceutical Corporation, Akebia's collaboration partner, submitted an NDA for treatment of anemia in dialysis and non-dialysis CKD patients in July 2019, and is awaiting an approval decision later in 2020. GSK is also conducting global Phase 3 studies in CKD patients on dialysis and not on dialysis, and expects to complete those studies by March 2022. GSK and Kyowa Hakko Kirin announced in November 2018 that the two companies signed a strategic commercialization deal in Japan for daprodustat. GSK submitted a Japan NDA for treatment of anemia in dialysis and non-dialysis in August 2019 and is awaiting approval later in 2020. Bayer has completed global Phase 2 studies and its HIF-PH inhibitor is now in Phase 3 development in CKD populations on dialysis and not on dialysis in Japan. Japan Tobacco submitted an NDA for treatment of anemia associated with CKD in Japan in November 2019, supported by the six Phase 3 studies conducted in CKD patients on dialysis and not on dialysis in Japan, and its partner JW Pharmaceuticals started a Phase 3 study in dialysis patients in Korea. Zydus Cadila (India) started Phase 3 studies in dialysis and non-dialysis CKD patients in India in 2019.

In addition, there are other companies developing biologic therapies for the treatment of other anemia indications that we may also seek to pursue in the future, including anemia of MDS. For example, Acceleron Pharma, Inc., in partnership with Celgene Corporation, a Bristol-Myers Squibb company ("Celgene"), developed Reblozyl® (luspatercept), a protein therapeutic, which was approved in November 2019 by the FDA for anemia treatment in patients with \(\beta\)-thalassemia. Its Biologics License Application ("BLA") under review by the FDA, for treatment of adult patients with very low to intermediate MDS associated anemia who have ring sideroblast and require red blood cell transfusions, has a Prescription Drug User Fee Act date of April 4, 2020. Acceleron expects an EMA decision on the MAA in the second half of 2020. In Japan, Celgene started a luspatercept Phase 2 study in May 2019. We may face competition for patient recruitment, enrollment for clinical trials, and potentially in commercial sales. There may also be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat if and when it is commercialized.

In China, biosimilars of epoetin alfa are offered by Chinese pharmaceutical companies such as EPIAO marketed by 3SBio Inc. as well as more than 15 other local manufacturers. We may also face competition by HIF-PH inhibitors from other companies such as Akebia, Bayer, and GSK, which was authorized by the National Medical Products Administration ("NMPA") to conduct trials in China to support its ex-China regulatory filings. Two domestic companies, Jiangsu Hengrui Medicine Co., Ltd. and Guandong Sunshine Health Investment Co., Ltd, have been permitted by the NMPA to conduct clinical trials for CKD anemia patients both on dialysis and not on dialysis, and 3SBio Inc. has submitted a clinical trial application to the NMPA to initiate trials for their HIF-PH inhibitor. Another domestic company, China Medical System, in-licensed desidustat, a compound which is currently in Phase 3 trials in India, from Zydus Candila for greater China in January 2020. Akebia announced in December 2015 that it had entered into a development and commercialization partnership with Mitsubishi Tanabe Pharmaceutical Corporation for its HIF-PH inhibitor vadadustat in Japan, Taiwan, South Korea, India and certain other countries in Asia, and announced in April 2017 an expansion of their U.S. collaboration with Otsuka to add markets, including China. 3SBio Inc. announced in 2016 its plan to begin a Phase 1 clinical trial of a HIF-PH inhibitor for the China market.

The first biosimilar ESA, Pfizer's Retacrit® (epoetin zeta), entered the U.S. market in November 2018. Market penetration of Retacrit and the potential addition of other biosimilar ESAs currently under development may alter the competitive and pricing landscape of anemia therapy in CKD patients on dialysis under the ESRD bundle. The patents for Amgen's EPOGEN® (epoetin alfa) expired in 2004 in the Europe, and the final material patents in the U.S. expired in May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in the Europe, China and other territories. In the U.S., a few ESA biosimilars are currently under development. Sandoz, a division of Novartis, markets Binocrit® (epoetin alfa) in Europe and may file a biosimilar BLA in the U.S.

The majority of the current CKD anemia market focuses on dialysis patients, who visit dialysis centers on a regular basis, typically three times a week, and anemia therapies are administered as part of the visit. Two of the largest operators of dialysis clinics in the U.S., DaVita Healthcare Partners Inc. ("DaVita"), and Fresenius Medical Care AG & Co. KGaA ("Fresenius"), collectively provide dialysis care to more than 80% of U.S. dialysis patients, and therefore have historically won long-term contracts including rebate terms with Amgen. DaVita has a six-year sourcing and supply agreement with Amgen effective through 2022. Fresenius' contract with Amgen expired in 2015, following which Fresenius is providing Roche's ESA Mircera® to a significant portion of its U.S. dialysis patients. Successful penetration in this market may require a significant agreement with Fresenius or DaVita, on favorable terms and on a timely basis.

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If approved and launched commercially to treat IPF, pamrevlumab is expected to compete with Roche's Esbriet® (pirfenidone), and Boehringer Ingelheim's Ofev® (nintedanib). We believe that if pamrevlumab can be shown to safely stabilize or reverse lung fibrosis, and thus stabilize or improve lung function in IPF patients, it can compete with pirfenidone and nintedanib for market share in IPF. However, it may be difficult to encourage treatment providers and patients to switch to pamrevlumab from a product they are already familiar with. We may also face competition from potential new IPF therapies in recruitment and enrollment in our clinical trials and potentially in commercialization.

Pamrevlumab is an injectable protein, which may be more expensive and less convenient than small molecules such as nintedanib and pirfenidone. Other potential competitive product candidates in various stages of development for IPF include Galapagos NV's GLPG1690 and GLPG1205, Kadmon Holdings, Inc.'s KD025, Liminal BioSciences' PBI-4050, and Roche/Promedior, Inc.'s PRM-151. In particular, GLPG1690 is in a Phase 3 program consisting of two clinical trials with 750 subjects each, intended to support both the U.S. NDA and MAA in Europe.

If pamrevlumab is approved and launched commercially to treat locally advanced pancreatic cancer patients who are not candidates for surgical resection, pamrevlumab may face competition from other products seeking approval in combination with gemcitibine and nab-paclitaxel, including FOLFRINOX, a combination chemotherapy regimen of folic acid, 5-fluouracil, oxaliplatin and irinotecan, and from companies such as Rafael Pharma's defactinib/CPI-613 and Merrimack's istiratumab. Gemcitabine and/or nab-paclitaxel are the current standard of care in the first-line treatment of metastatic pancreatic cancer. Celgene Corporation's Abraxane® (nab-paclitaxel) was launched in the U.S. and Europe in 2013 and 2014, and was the first drug approved in this disease in nearly a decade.

If approved and launched commercially to treat DMD, pamrevlumab is expected to face competition from drugs that have been approved in major markets such as the U.S., EU, and Japan. On September 19, 2016, the FDA approved Sarepta Therapeutics Inc.'s ("Sarepta") Exondys 51TM (eteplirsen). This was the first drug approved to treat DMD. Exondys 51 is approved to treat patients who have a mutation of the dystrophin gene amenable to exon 51 skipping, representing approximately 13% of patients with DMD. In Europe, Sarepta received a negative opinion for its marketing application for eteplirsen from the EMA in September 2018. Sarepta has reported a full year Exondys 51 revenue of \$380 million in 2019. Sarepta's Vyondys 53TM (golodirsen) was also approved by the FDA in December 2019 for patients with a confirmed genetic mutation that is amenable to exon 53 skipping, which accounts for 8% of the DMD population.

PTC Therapeutics' product Translarna TM received a conditional approval in Europe in 2014, which was renewed in November 2016 with a request for a new randomized placebo-controlled 18-month study by the Committee for Medicinal Products for Human Use of the EMA; however, the FDA informed the sponsor in a complete response letter in October 2017, as well as in its response to PTC Therapeutics' appeal, that the FDA is unable to approve the application in its current form. While Translarna TM targets a different set of DMD patients from those targeted by Sarepta's Exondys 51®, it is also limited to a subset of patients who carry a specific mutation. Conversely, pamrevlumab is intended to treat DMD patients without limitation to type of mutation.

Pamrevlumab may also face competition from other drugs currently in clinical development in patient recruiting and enrollment in clinical trials, and, if approved, in commercialization. Examples of those compounds currently under clinical development are the drug candidates from Catabasis Pharmaceuticals ("Catabasis"), Santhera Pharmaceuticals ("Santhera") and Sarepta. Catabasis' edasalonexent was reported to have preserved muscle function and slowed the progression of DMD compared to rates of change in the control period prior to treatment with edasalonexent in a Phase 2 study, and is currently undergoing Phase 3 development. Santhera's Puldysa® (idebenone) MAA for treatment of DMD was filed with the EMA, and the opinion from the Committee for Medicinal Products for Human Use is expected in the second quarter of 2020. The FDA requested additional clinical data from the idebenone Phase 3 trial currently ongoing in the U.S. and Europe. Santhera offers compassionate use of idebenone in patients with DMD in U.S. and UK. Sarepta's SRP-9001 is an investigational gene therapy for DMD. Sarepta announced in December 2019 the licensing agreement with Roche that grants Roche the commercial rights to SRP-9001 outside the U.S.

The success of any or all of these potential competitive products may negatively impact the development and potential for success of pamrevlumab. In addition, any competitive products that are on the market or in development may compete with pamrevlumab for patient recruitment and enrollment for clinical trials or may force us to change our clinical trial design, including, in order to compare pamrevlumab against another drug, which may be the new standard of care.

Moreover, many of our competitors have significantly greater resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients, manufacturing pharmaceutical products, and commercialization. In the potential anemia market for roxadustat, for example, large and established companies such as Amgen and Roche, among others, compete aggressively to maintain their market shares. In particular, the currently marketed ESA products are supported by large pharmaceutical companies that have greater experience and expertise in commercialization in the anemia market, including in securing reimbursement, government contracts and relationships with key opinion leaders; conducting testing and clinical trials; obtaining and maintaining regulatory approvals and distribution relationships to market products; and marketing approved products. These companies also have significantly greater scale, research and marketing capabilities than we do and may also have products that have been approved or are in later stages of development and have collaboration agreements in our target markets with leading dialysis companies and research institutions. These competitors have in the past successfully prevented new and competing products from entering the anemia market, and we expect that their resources will represent challenges for us and our collaboration partners, AstraZeneca and Astellas. If we and our collaboration partners are not able to compete effectively against existing and potential competitors, our business and financial condition may be materially and adversely affected.

No or limited reimbursement or insurance coverage of our approved products, if any, by third-party payors may render our products less attractive to patients and healthcare providers.

Market acceptance and sales of any approved products will depend significantly on reimbursement or coverage of our products by government or third-party payors and may be affected by existing and future healthcare reform measures or prices of related products for which the government or third-party reimbursement applies. Coverage and reimbursement by the government or a third-party payor may depend upon a number of factors, including the payor's determination that use of a product is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- · cost-effective; and
- · neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor, which we may not be able to provide. Furthermore, the reimbursement policies of third-party payors may significantly change in a manner that renders our clinical data insufficient for adequate reimbursement or otherwise limits the successful marketing of our products. Even if we obtain coverage for our product candidates, third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. For example, the initial roxadustat reimbursement prices set by the Ministry of Health, Labour and Welfare in Japan in November 2019 did not reflect innovation premium over the current ESA therapy, despite roxadustat's advantages observed in our clinical programs. We believe the Japanese authority's decision was primarily based on the comparability of roxadustat shown in the Japan Phase 3 studies which supported the Japan NDA, that was not designed to evaluate the outcome and additional efficacy and safety data observed in the large global Phase 3 programs that included over 8,000 patients. We have no control over whether the agency will revisit the pricing once they review the comprehensive data from the global Phase 3 program including the MACE/MACE+ outcomes. If reimbursement is not available or is available only to limited levels or only in subsets of the dialysis and non-dialysis populations, we may not be able to successfully commercialize certain of our products, or in particular jurisdictions.

Price controls may limit the price at which products such as roxadustat, if approved, are sold. For example, reference pricing is used by various Europe member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partner may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unacceptable levels, we or our partner may elect not to commercialize our products in such countries, and our business and financial condition could be adversely affected.

Risks Related to Our Reliance on Third Parties

If our collaborations with our collaboration partners Astellas or AstraZeneca were terminated, if Astellas or AstraZeneca were to prioritize other initiatives over their collaborations with us, whether as a result of a change of control or otherwise, if conflicts arise between us and Astellas or AstraZeneca, or if Astellas or AstraZeneca becomes our competitor in the future, our ability to successfully develop and commercialize our product candidates would suffer.

We have entered into collaboration agreements with respect to the development and commercialization of our lead product candidate, roxadustat, with our collaboration partners Astellas and AstraZeneca. These agreements provide for reimbursement of our development costs by our collaboration partners and also provide for commercialization of roxadustat throughout the major territories of the world.

Our agreements with Astellas and AstraZeneca provide each of them with the right to terminate their respective agreements with us, upon the occurrence of negative clinical results, delays in the development and commercialization of our product candidates or adverse regulatory requirements or guidance. The termination of any of our collaboration agreements would require us to fund and perform the further development and commercialization of roxadustat in the affected territory, or pursue another collaboration, which we may be unable to do, either of which could have an adverse effect on our business and operations. In addition, each of those agreements provides our respective partners the right to terminate any of those agreements upon written notice for convenience. Moreover, if Astellas or AstraZeneca, or any successor entity, were to determine that their collaborations with us are no longer a strategic priority, or if either of them or a successor were to reduce their level of commitment to their collaborations with us, our ability to develop and commercialize roxadustat could suffer. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaboration agreements with other parties in the area or field of exclusivity.

If we fail to establish and maintain strategic collaborations related to our product candidates, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise at significant cost. This in turn may negatively affect the development of our other product candidates as we direct resources to our most advanced product candidates.

Our collaboration partners also have certain rights to control decisions regarding the development and commercialization of our product candidates with respect to which they are providing funding. If we have a disagreement over strategy and activities with our collaboration partners, our plans for obtaining approval may be revised and negatively affect the anticipated timing and potential for success of our product candidates. Even if a product under a collaboration agreement is approved, we will remain substantially dependent on the commercialization strategy and efforts of our collaboration partners, and neither of our collaboration partners has experience in commercialization of a novel drug such as roxadustat in the dialysis market.

With respect to our collaboration agreements for roxadustat, there are additional complexities in that we and our collaboration partners, Astellas and AstraZeneca, must reach consensus on our regulatory activities, including for the NDA in the U.S. and the Marketing Authorization Application in Europe. Multi-party decision-making is complex and involves significant time and effort, and there can be no assurance that the parties will cooperate or reach consensus, or that one or both of our partners will not ask to proceed independently in some or all of their respective territories or functional areas of responsibility in which the applicable collaboration partner would otherwise be obligated to cooperate with us. Any disputes or lack of cooperation with us by either Astellas or AstraZeneca may negatively impact the timing or success of our regulatory approval applications.

We intend to conduct proprietary research programs in specific disease areas that are not covered by our collaboration agreements. Our pursuit of such opportunities could, however, result in conflicts with our collaboration partners in the event that any of our collaboration partners takes the position that our internal activities overlap with those areas that are exclusive to our collaboration agreements. Moreover, disagreements with our collaboration partners could develop over rights to our intellectual property. In addition, our collaboration agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaboration partners could lead to the termination of our collaboration agreements, delay collaborative activities, reduce our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaboration partners.

Certain of our collaboration partners could also become our competitors in the future. If our collaboration partners develop competing products, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our product candidates, the development and commercialization of our product candidates and products could be delayed.

We rely on third parties for the conduct of most of our preclinical and clinical trials for our product candidates, and if our third-party contractors do not properly and successfully perform their obligations under our agreements with them, we may not be able to obtain or may be delayed in receiving regulatory approvals for our product candidates.

We rely heavily on university, hospital, dialysis centers and other institutions and third parties, including the principal investigators and their staff, to carry out our clinical trials in accordance with our clinical protocols and designs. We also rely on a number of third-party CROs to assist in undertaking, managing, monitoring and executing our ongoing clinical trials, including those for roxadustat. We expect to continue to rely on CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our development efforts in the future, including our Phase 3 development program for roxadustat. We compete with many other companies for the resources of these third parties, and large pharmaceutical companies often have significantly more extensive agreements and relationships with such third-party providers, and such third-party providers may prioritize the requirements of such large pharmaceutical companies over ours. The third parties on whom we rely may terminate their engagements with us at any time, which may cause delay in the development and commercialization of our product candidates. If any such third party terminates its engagement with us or fails to perform as agreed, we may be required to enter into alternative arrangements, which would result in significant cost and delay to our product development program. Moreover, our agreements with such third parties generally do not provide assurances regarding employee turnover and availability, which may cause interruptions in the research on our product candidates by such third parties.

Moreover, while our reliance on these third parties for certain development and management activities will reduce our control over these activities, it will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP requirements for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results from trials are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we, as the sponsor, remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites.

If any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, other regulations, trial protocol or other requirements under their agreements with us, the quality or accuracy of the data they obtain may be compromised or unreliable, and the trials of our product candidates may not meet regulatory requirements. If trials do not meet regulatory requirements or if these third parties need to be replaced, the development of our product candidates may be delayed, suspended or terminated, regulatory authorities may require us to exclude the use of patient data from our approval applications or perform additional clinical trials before approving our marketing applications. Regulatory authorities may even reject our application for approval or refuse to accept our future applications for an extended time period. We cannot assure that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements or that our results may be used in support of our regulatory submissions. If any of these events occur, we may not be able to obtain regulatory approval for our product candidates on a timely basis, at a reasonable cost, or at all.

We currently rely, and expect to continue to rely, on third parties to conduct many aspects of our product manufacturing and distribution, and these third parties may not perform satisfactorily.

We do not have operating manufacturing facilities at this time other than our roxadustat manufacturing facility in China, and our current commercial manufacturing facility plans in China are not expected to satisfy the requirements necessary to support development and commercialization outside of China. Other than in and for China specifically, we do not expect to independently manufacture our products. We currently rely, and expect to continue to rely, on third parties to scale-up, manufacture and supply roxadustat and our other product candidates outside of China. We also rely entirely on third parties for distribution in China. Risks arising from our reliance on third-party manufacturers include:

- reduced control and additional burdens of oversight as a result of using third-party manufacturers and distributors for all aspects of
 manufacturing activities, including regulatory compliance and quality control and quality assurance;
- termination of manufacturing agreements, termination fees associated with such termination, or nonrenewal of manufacturing
 agreements with third parties may negatively impact our planned development and commercialization activities;
- · the possible misappropriation of our proprietary technology, including our trade secrets and know-how; and
- disruptions to the operations of our third-party manufacturers, distributors or suppliers unrelated to our product, including the merger, acquisition, or bankruptcy of a manufacturer or supplier or a catastrophic event affecting our manufacturers, distributors or suppliers.

Any of these events could lead to development delays or failure to obtain regulatory approval or affect our ability to successfully commercialize our product candidates. Some of these events could be the basis for action by the FDA or another regulatory authority, including injunction, recall, seizure or total or partial suspension of production.

The facilities used by our contract manufacturer to manufacture our product candidates must pass inspections by the FDA and other regulatory authorities. Although, except for China, we do not control the manufacturing operations of, and expect to remain completely dependent on, our contract manufacturers for manufacture of drug substance and finished drug product, we are ultimately responsible for ensuring that our product candidates are manufactured in compliance with cGMP requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our or our collaboration partners' specifications, or the regulatory requirements of the FDA or other regulatory authorities, we may not be able to secure and/or maintain regulatory approval for our product candidates and our development or commercialization plans may be delayed. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. In addition, although our longer-term agreements are expected to provide for requirements to meet our quantity and quality requirements to manufacture our products candidates for clinical studies and commercial sale, we will have minimal direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel and we expect to rely on our audit rights to ensure that those qualifications are maintained to meet our requirements. If our contract manufacturers' facilities do not pass inspection by regulatory authorities, or if regulatory authorities do not approve these facilities for the manufacture of our products, or withdraw any such approval in the future, we would need to identify and qualify alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products, if approved. Moreover, any failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or adverse regulatory consequences, including clinical holds, warnings or untitled letters, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which would be expected to significantly and adversely affect supplies of our products to us and our collaboration partners.

Other than for Catalent, our commercial third-party supplier of roxadustat drug product in the U.S. and Europe, most of our other third-party manufacturers may terminate their engagement with us at any time and we have not yet entered into any commercial supply agreements for the manufacture of drug substance or active pharmaceutical ingredient ("API") or drug products. With respect to roxadustat, AstraZeneca and Astellas have certain rights to assume manufacturing of roxadustat and the existence of those rights may limit our ability to enter into favorable long-term supply agreements, if at all, with other third-party manufacturers. In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access and prioritization to manufacture. Certain third-party manufacturers may be contractually prohibited from manufacturing our product due to non-compete agreements with our competitors or a commitment to grant another party priority relative to our products. There are a limited number of third-party manufacturers that operate under cGMP and that might be capable of manufacturing to meet our requirements. Due to the limited number of third-party manufacturers with the contractual freedom, expertise, required regulatory approvals and facilities to manufacture our products on a commercial scale, identifying and qualifying a replacement third-party manufacturer would be expensive and time-consuming and may cause delay or interruptions in the production of our product candidates or products, which in turn may delay, prevent or impair our development and commercialization efforts.

We have a letter agreement with IRIX Pharmaceuticals, Inc. ("IRIX"), a third-party manufacturer that we have used in the past, pursuant to which we agreed to negotiate a single source manufacturing agreement that included a right of first negotiation for the cGMP manufacture of HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third-party bids within 5%. The exclusive right to manufacture extends for five years after approval of an NDA for those compounds, and any agreement would provide that no minimum amounts would be specified until appropriate by forecast and that we and a commercialization partner would have the rights to contract with independent third parties that exceed IRIX's internal manufacturing capabilities or in the event that we or our commercialization partner determines for reasons of continuity of supply and security that such a need exists, provided that IRIX would supply no less than 65% of the product if it is able to provide this level of supply. Subsequent to the letter agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the letter agreement with respect to the single source manufacturing agreement, and if we were to enter into any such exclusive manufacturing agreement, there can be no assurance that IRIX will not assert a claim for right to manufacture roxadustat or that IRIX could manufacture roxadustat successfully and in accordance with applicable regulations for a commercial product and the specifications of our collaboration partners. In 2015, Patheon Pharmaceuticals Inc., a business unit of DPx Holdings B.V. ("Patheon"), acquired IRIX, and in 2017 ThermoFisher Scientific Inc. acquired Patheon.

If any third-party manufacturer terminates its engagement with us or fails to perform as agreed, we may be required to find replacement manufacturers, which would result in significant cost and delay to our development programs. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such third party or potential second source manufacturer. In any event, with any third-party manufacturer we expect to enter into technical transfer agreements and share our know-how with the third-party manufacturer, which can be time-consuming and may result in delays. These delays could result in a suspension or delay of marketing roxadustat.

Certain of the components of our product candidates are acquired from single-source suppliers and have been purchased without long-term supply agreements. The loss of any of these suppliers, or their failure to supply us with supplies of sufficient quantity and quality to complete our drug substance or finished drug product of acceptable quality and an acceptable price, would materially and adversely affect our business.

We do not have an alternative supplier of certain components of our product candidates. We may be unable to enter into long-term commercial supply arrangements for some of our products, or do so on commercially reasonable terms, which could have a material adverse impact upon our business. In addition, we currently rely on our contract manufacturers to purchase from third-party suppliers some of the materials necessary to produce our product candidates. We do not have direct control over the acquisition of those materials by our contract manufacturers.

The logistics of our supply chain, which include shipment of materials and intermediates from countries such as China and India add additional time and risk (including risk of loss) to the manufacture of our product candidates. While we have in the past maintained sufficient inventory of materials, API, and drug product to meet our and our collaboration partners' needs for roxadustat to date, the lead time and regulatory approvals required to source from and into countries outside of the U.S. increase the risk of delay and potential shortages of supply.

Risks Related to Our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection, and contractual arrangements to protect the intellectual property related to our technologies. We will only be able to protect our products and proprietary information and technology by preventing unauthorized use by third parties to the extent that our patents, trade secrets, and contractual position allow us to do so. Any disclosure to or misappropriation by third parties of our trade secrets or confidential information could compromise our competitive position. Moreover, we are involved in, have in the past been involved in, and may in the future be involved in legal or administrative proceedings involving our intellectual property initiated by third parties, and which proceedings can result in significant costs and commitment of management time and attention. As our product candidates continue in development, third parties may attempt to challenge the validity and enforceability of our patents and proprietary information and technologies.

We also are involved in, have in the past been involved in, and may in the future be involved in initiating legal or administrative proceedings involving the product candidates and intellectual property of our competitors. These proceedings can result in significant costs and commitment of management time and attention, and there can be no assurance that our efforts would be successful in preventing or limiting the ability of our competitors to market competing products.

Composition-of-matter patents relating to the API are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection not limited to any one method of use. Method-of-use patents protect the use of a product for the specified method(s), and do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. We rely on a combination of these and other types of patents to protect our product candidates, and there can be no assurance that our intellectual property will create and sustain the competitive position of our product candidates.

Biotechnology and pharmaceutical product patents involve highly complex legal and scientific questions and can be uncertain. Any patent applications that we own or license may fail to result in issued patents. Even if patents do successfully issue from our applications, third parties may challenge their validity or enforceability, which may result in such patents being narrowed, invalidated, or held unenforceable. Even if our patents and patent applications are not challenged by third parties, those patents and patent applications may not prevent others from designing around our claims and may not otherwise adequately protect our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, competitors with significantly greater resources could threaten our ability to commercialize our product candidates. Discoveries are generally published in the scientific literature well after their actual development, and patent applications in the U.S. and other countries are typically not published until 18 months after their filing, and in some cases are never published. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or patent applications, or that we or our licensors were the first to file for patent protection covering such inventions. Subject to meeting other requirements for patentability, for U.S. patent applications filed prior to March 16, 2013, the first to invent the claimed invention is entitled to receive patent protection for that invention while, outside the U.S., the first to file a patent application encompassing the invention is entitled to patent protection for the invention. The U.S. moved to a "first to file" system under the Leahy-Smith America Invents Act, effective March 16, 2013. This system also includes procedures for challenging issued patents and pending patent applications, which creates additional uncertainty. We may become involved in opposition or interference proceedings challenging our patents and patent applications or the patents and patent applications of others, and the outcome of any such proceedings are highly uncertain. An unfavorable outcome in any such proceedings could reduce the scope of or invalidate our patent rights, allow third parties to commercialize our technology and compete directly with us, or result in our inability to manufacture, develop or commercialize our product candidates without infringing the patent rights of others.

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In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to assign their inventions to us, and we require all of our employees, consultants, advisors and any third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how and other information and technology. Furthermore, the laws of some foreign countries, in particular, China, where we have operations, do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business and operations.

Intellectual property disputes with third parties and competitors may be costly and time consuming, and may negatively affect our competitive position.

Our commercial success may depend on our avoiding infringement of the patents and other proprietary rights of third parties as well as on enforcing our patents and other proprietary rights against third parties. Pharmaceutical and biotechnology intellectual property disputes are characterized by complex, lengthy and expensive litigation over patents and other intellectual property rights. We may initiate or become party to or be threatened with future litigation or other proceedings regarding intellectual property rights with respect to our product candidates and competing products.

As our product candidates progress toward commercialization, we or our collaboration partners may be subject to patent infringement claims from third parties. We attempt to ensure that our product candidates do not infringe third-party patents and other proprietary rights. However, the patent landscape in competitive product areas is highly complex, and there may be patents of third parties of which we are unaware that may result in claims of infringement. Accordingly, there can be no assurance that our product candidates do not infringe proprietary rights of third parties, and parties making claims against us may seek and obtain injunctive or other equitable relief, which could potentially block further efforts to develop and commercialize our product candidates including roxadustat or pamrevlumab. Any litigation involving defense against claims of infringement, regardless of the merit of such claims, would involve substantial litigation expense and would be a substantial diversion of management time.

We may consider administrative proceedings and other means for challenging third-party patents and patent applications. An unfavorable outcome in any such challenge could require us to cease using the related technology and to attempt to license rights to it from the prevailing third party, which may not be available on commercially reasonable terms, if at all, in which case our business could be harmed.

We intend, if necessary, to vigorously enforce our intellectual property in order to protect the proprietary position of our product candidates, including roxadustat and pamrevlumab. In addition, our collaboration partners who have been granted licenses to our patents may also have rights related to enforcement of those patents. Active efforts to enforce our patents by us or by our partners may include litigation, administrative proceedings, or both, depending on the potential benefits that might be available from those actions and the costs associated with undertaking those efforts against third parties. We carefully review and monitor publicly available information regarding products that may be competitive with our product candidates and assert our intellectual property rights where appropriate. For example, we previously prevailed in an administrative challenge initiated by a major biopharmaceutical company regarding our intellectual property rights, maintaining our intellectual property in all relevant scope, and will continue to protect and enforce our intellectual property rights. In addition, our partner Astellas initiated *quia timet* infringement actions against Akebia and GSK based on our specific patents in the United Kingdom in response to actions taken by Akebia and GSK against those patents, as further detailed below.

Third parties may also challenge our patents and patent applications, through interference, reexamination, inter partes review, and post-grant review proceedings before the U.S. Patent and Trademark Office ("USPTO") or through comparable proceedings in other territories. For example, Akebia and others have filed oppositions against certain European patents within our HIF anemia-related technologies patent portfolio. In three of these proceedings, for FibroGen European Patent Nos. 1463823, 1633333, and 2322155, the European Patent Office has handed down decisions unfavorable to FibroGen. In a fourth of these proceedings, the European Patent Office issued a decision favorable to FibroGen, maintaining FibroGen European Patent No. 2322153 in amended form. All of these decisions are currently under appeal, and these four patents are valid and enforceable pending resolution of the appeals. The ultimate outcomes of such proceedings remain uncertain, and ultimate resolution of the appeals may take considerable time. In addition, Akebia has filed oppositions against FibroGen European Patent Nos. 2289531 and 2298301. As mentioned above, Akebia and GSK initiated invalidation actions in the United Kingdom against the United Kingdom counterparts of each of these European patents, and GSK has filed for a declaration of non-infringement of certain United Kingdom patents (corresponding to FibroGen European Patent Nos. 2322153 and 2322155) with respect to its daprodustat product. We have reached a settlement agreement with GSK to resolve the actions to which GSK is/was a party, resulting in dismissal of the UK court actions as well as the proceedings filed by GSK against the patents in the EPO. Astellas' proceedings brought against GSK on a quia timet basis have also been dismissed as a result of the settlement agreement. Akebia is also pursuing invalidation actions against corresponding patents in Canada and in Japan. While we believe the ultimate outcome of all proceedings will be that these FibroGen patents will be upheld in relevant part, we note that narrowing or even revocation of any of these patents would not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia.

Oppositions have also recently been filed against our European Patent No. 2872488, which claims a crystalline form of roxadustat. Final resolution of the opposition proceedings will take considerable time, and we cannot be assured of the breadth of the claims that will remain in the '488 Patent or that the patent will not be revoked in its entirety.

Furthermore, there is a risk that any public announcements concerning the status or outcomes of intellectual property litigation or administrative proceedings may adversely affect the price of our stock. If securities analysts or our investors interpret such status or outcomes as negative or otherwise creating uncertainty, our common stock price may be adversely affected.

Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.

Our reliance on third-party contractors to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our trade secrets and know-how. Despite the contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations in place with our collaboration partners. Despite our efforts to protect our trade secrets and other confidential information, a competitor's discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

We have an extensive worldwide patent portfolio. The cost of maintaining our patent protection is high and maintaining our patent protection requires continuous review and compliance in order to maintain worldwide patent protection. We may not be able to effectively maintain our intellectual property position throughout the major markets of the world.

The USPTO and foreign patent authorities require maintenance fees and payments as well as continued compliance with a number of procedural and documentary requirements. Noncompliance may result in abandonment or lapse of the subject patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance may result in reduced royalty payments for lack of patent coverage in a particular jurisdiction from our collaboration partners or may result in competition, either of which could have a material adverse effect on our business.

We have made, and will continue to make, certain strategic decisions in balancing costs and the potential protection afforded by the patent laws of certain countries. As a result, we may not be able to prevent third parties from practicing our inventions in all countries throughout the world, or from selling or importing products made using our inventions in and into the U.S. or other countries. Third parties may use our technologies in territories in which we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories which provide inadequate enforcement mechanisms, even if we have patent protection. Such third-party products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the U.S., and we may encounter significant problems in securing and defending our intellectual property rights outside the U.S.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries, particularly certain developing countries such as China, do not always favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop infringement of our patents, misappropriation of our trade secrets, or marketing of competing products in violation of our proprietary rights. In China, our intended establishment of significant operations will depend in substantial part on our ability to effectively enforce our intellectual property rights in that country. Proceedings to enforce our intellectual property rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, and could put our patents in these territories at risk of being invalidated or interpreted narrowly, or our patent applications at risk of not being granted, and could provoke third parties to assert claims against us. We may not prevail in all legal or other proceedings that we may initiate and, if we were to prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Intellectual property rights do not address all potential threats to any competitive advantage we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and intellectual property rights may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- The prosecution of our pending patent applications may not result in granted patents.
- Granted patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid
 or unenforceable, as a result of legal challenges by our competitors.
- Patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product.
- Our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from
 patent infringement claims for such activities, as well as in countries in which we do not have patent rights, and may then use the
 information learned from such activities to develop competitive products for sale in markets where we intend to market our product
 candidates.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold or used for research under the same or similar names, or similar mechanism of action or product class, but which are sold without proper licenses or approvals, and are often lower cost, lower quality, different potency, or have different ingredients or formulations, and have the potential to damage the reputation for quality and effectiveness of the genuine product. Such products may be used for indications or purposes that are not recommended or approved or for which there is no data or inadequate data with regard to safety or efficacy. Such products divert sales from genuine products. If counterfeit pharmaceuticals illegally sold or used for research result in adverse events or side effects to consumers, we may be associated with any negative publicity resulting from such incidents. Consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. In addition, the use of counterfeit products could be used in non-clinical or clinical studies, or could otherwise produce undesirable side effects or adverse events that may be attributed to our products as well, which could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for the commercialization of our product candidates.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. Except for roxadustat in China for patients on dialysis and not on dialysis, and Japan for patients on dialysis, we have not obtained regulatory approval for any product candidate, and it is possible that neither roxadustat nor pamrevlumab, nor any future product candidates we may discover, in-license or acquire and seek to develop in the future, will obtain regulatory approval in additional countries.

Our product candidates could fail to receive regulatory approval from the FDA or other regulatory authorities for many reasons, including:

- disagreement over the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement over our interpretation of data from preclinical studies or clinical trials;
- disagreement over whether to accept efficacy results from clinical trial sites outside the U.S. where the standard of care is potentially different from that in the U.S.;
- the insufficiency of data collected from clinical trials of our present or future product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- disapproval of the manufacturing processes or facilities of either our manufacturing plant or third party manufacturers with whom we contract for clinical and commercial supplies; or
- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or other regulatory authorities may require more information, including additional preclinical or clinical data to support approval, or different analyses, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program altogether. Even if we do obtain regulatory approval, our product candidates may be approved for fewer or more limited indications than we request, approval may be contingent on the performance of costly post-marketing clinical trials, or approval may require labeling that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS or other regulatory authorities may require the establishment of a similar strategy, that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we believe our clinical trials are successful, regulatory authorities may not agree that our completed clinical trials provide adequate data on safety or efficacy. Approval by one regulatory authority does not ensure approval by any other regulatory authority. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for regulatory approvals and even if we file we may not receive the necessary approvals to commercialize our product candidates in any market.

Our relationships with customers, physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain approval in the U.S. for any of our product candidates, the regulatory requirements applicable to our operations, in particular our sales and marketing efforts, will increase significantly with respect to our operations and the potential for civil and criminal enforcement by the federal government and the states and foreign governments will increase with respect to the conduct of our business. The laws that may affect our operations in the U.S. include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving,
 offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service
 reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes
 certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Patient Protection and Affordable Care Act ("PPACA"), which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare and Medicaid Services ("CMS"), information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;

- foreign and state law equivalents of each of the above federal laws, such as the U.S. Foreign Corrupt Practices Act ("FCPA"), anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and
- the Trade Agreements Act ("TAA"), which requires that drugs sold to the U.S. Government must be manufactured in the U.S. or in TAA approved and designated countries. Drugs manufactured in countries not approved under the TAA, may not be sold to the U.S. without specific regulatory approval. We have little experience with this regulation and there is a risk that drugs made from Chinesemade API may not be sold to an entity of the U.S. such as the Veterans Health Administration ("VA") due to our inability to obtain regulatory approval. While there have been recent VA policy changes that appear to allow for sale of drugs from non-TAA approved countries, this policy may change or there may be additional policies or legislation that affect our ability to sell drug to the U.S. Government

The scope of these laws and our lack of experience in establishing the compliance programs necessary to comply with this complex and evolving regulatory environment increases the risks that we may unknowingly violate the applicable laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results.

Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have a material adverse effect on our ability to compete in the marketplace.

We are subject to laws and regulations governing corruption, which will require us to develop, maintain, and implement costly compliance programs.

We must comply with a wide range of laws and regulations to prevent corruption, bribery, and other unethical business practices, including the FCPA, anti-bribery and anti-corruption laws in other countries, particularly China. The implementation and maintenance of compliance programs is costly and such programs may be difficult to enforce, particularly where reliance on third parties is required.

Anti-bribery laws prohibit us, our employees, and some of our agents or representatives from offering or providing any personal benefit to covered government officials to influence their performance of their duties or induce them to serve interests other than the missions of the public organizations in which they serve. Certain commercial bribery rules also prohibit offering or providing any personal benefit to employees and representatives of commercial companies to influence their performance of their duties or induce them to serve interests other than their employers. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with these anti-bribery laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the anti-bribery laws present particular challenges in the pharmaceutical industry because in many countries including China, hospitals are state-owned or operated by the government, and doctors and other hospital employees are considered foreign government officials. Furthermore, in certain countries (China in particular), hospitals and clinics are permitted to sell pharmaceuticals to their patients and are primary or significant distributors of pharmaceuticals. Certain payments to hospitals in connection with clinical studies, procurement of pharmaceuticals and other work have been deemed to be improper payments to government officials that have led to vigorous anti-bribery law enforcement actions and heavy fines in multiple jurisdictions, particularly in the U.S. and China.

It is not always possible to identify and deter violations, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

In the pharmaceutical industry, corrupt practices include, among others, acceptance of kickbacks, bribes or other illegal gains or benefits by the hospitals and medical practitioners from pharmaceutical manufacturers, distributors or their third-party agents in connection with the prescription of certain pharmaceuticals. If our employees, affiliates, distributors or third-party marketing firms violate these laws or otherwise engage in illegal practices with respect to their sales or marketing of our products or other activities involving our products, we could be required to pay damages or heavy fines by multiple jurisdictions where we operate, which could materially and adversely affect our financial condition and results of operations. The Chinese government has also sponsored anti-corruption campaigns from time to time, which could have a chilling effect on any future marketing efforts by us to new hospital customers. There have been recent occurrences in which certain hospitals have denied access to sales representatives from pharmaceutical companies because the hospitals wanted to avoid the perception of corruption. If this attitude becomes widespread among our potential customers, our ability to promote our products to hospitals may be adversely affected.

As we expand our operations in China and other jurisdictions internationally, we will need to increase the scope of our compliance programs to address the risks relating to the potential for violations of the FCPA and other anti-bribery and anti-corruption laws. Our compliance programs will need to include policies addressing not only the FCPA, but also the provisions of a variety of anti-bribery and anti-corruption laws in multiple foreign jurisdictions, including China, provisions relating to books and records that apply to us as a public company, and include effective training for our personnel throughout our organization. The creation and implementation of anti-corruption compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. Violation of the FCPA and other anti-corruption laws can result in significant administrative and criminal penalties for us and our employees, including substantial fines, suspension or debarment from government contracting, prison sentences, or even the death penalty in extremely serious cases in certain countries. The SEC also may suspend or bar us from trading securities on U.S. exchanges for violation of the FCPA's accounting provisions. Even if we are not ultimately punished by government authorities, the costs of investigation and review, distraction of our personnel, legal defense costs, and harm to our reputation could be substantial and could limit our profitability or our ability to develop or commercialize our product candidates. In addition, if any of our competitors are not subject to the FCPA, they may engage in practices that will lead to their receipt of preferential treatment from foreign hospitals and enable them to secure business from foreign hospitals in ways that are unavailable to us.

The impact of recent U.S. healthcare reform, its potential partial or full repeal, and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.

The commercial potential for our approved products could be affected by changes in healthcare spending and policy in the U.S. and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") altered Medicare coverage and payments for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. The MMA also provided authority for limiting the number of drugs that will be covered in any therapeutic class and as a result, we expect that there will be additional pressure to reduce costs. For example, the CMS in implementing the MMA has enacted regulations that reduced capitated payments to dialysis providers. These cost reduction initiatives and other provisions of the MMA could decrease the scope of coverage and the price that may be received for any approved dialysis products and could seriously harm our business and financial condition. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies have been enacted in many international markets which could similarly impact the commercial potential for our products.

Under the Medicare Improvements for Patients and Providers Act ("MIPPA"), a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by the CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage. It is unknown whether roxadustat, if approved in the U.S., will be included in the payment bundle. Under MIPPA, agents that have no IV equivalent in the bundle are currently expected to be excluded from the bundle until 2025. If roxadustat were included in the bundle, it may reduce the price that could be charged for roxadustat, and therefore potentially limit our profitability. Based on roxadustat's differentiated mechanism of action and therapeutic effects, and discussions with our collaboration partner, we currently believe that roxadustat might not be included in the bundle. If roxadustat is reimbursed outside of the bundle, it may potentially limit or delay market penetration of roxadustat.

In March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, (collectively, the "PPACA"), was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the U.S. There remain judicial and Congressional challenges to certain aspects of the PPACA as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA. For example, the Tax Cuts and Jobs Act of 2017, (the "Tax Act"), was enacted, which includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Additionally, on December 15, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA and our business.

Further, in the U.S. there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. At the federal level, the Trump administration's budget proposals for fiscal year 2020 contains further drug price control measures that could be enacted during the budget process or in other future legislation. In addition, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services has solicited feedback on some of these measures and has implemented others under its existing authority. While some of these measures may require additional authorization to become effective, the U.S. Congress and the Trump administration have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that additional U.S. healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for any future products or additional pricing pressures.

Roxadustat is considered a Class 2 substance on the 2019 World Anti-Doping Agency Prohibited List which could limit sales and increase security and distribution costs for us and our partners, particularly in China.

Roxadustat is considered a Class 2 substance on the World Anti-Doping Agency ("WADA") Prohibited List. There are enhanced security and distribution procedures we and our collaboration partners and third-party contractors will have to take to limit the risk of loss of product in the supply chain. As a result, our distribution, manufacturing and sales costs for roxadustat, as well as for our partners, will be increased which will reduce profitability. In addition, there is a risk of reduced sales due to patient access to this drug. This is particularly the case in China where we will not be able to sell roxadustat in private pharmacies due to the WADA classification. While private pharmacies only represent approximately 10% of the market in China, this will negatively affect sales and therefore the profitability of roxadustat and the Company as a whole.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could result in significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failure to:

- · comply with FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or comparable foreign regulatory authorities;
- comply with manufacturing standards we have established;
- comply with privacy laws protecting personal information;
- comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities;
- comply with the FCPA and other anti-bribery laws;
- report financial information or data accurately;
- or disclose unauthorized activities to us.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, delays in clinical trials, or serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could harm our business, results of operations, financial condition and cash flows, including through the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations applicable to our operations in the U.S. and foreign countries. These current or future laws and regulations may impair our research, development or manufacturing efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our International Operations

We are establishing international operations and seeking approval to commercialize our product candidates outside of the U.S., in particular in China, and a number of risks associated with international operations could materially and adversely affect our business.

We expect to be subject to a number of risks related with our international operations, many of which may be beyond our control. These risks include:

- different regulatory requirements for drug approvals in different countries;
- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain countries;

- changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems and different competitive drugs indicated to treat the indications for which our product candidates are being developed;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- · compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- · compliance with the FCPA, and other anti-corruption and anti-bribery laws;
- U.S. and foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating costs and expenses and reduced revenues, and other
 obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- · production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- a reliance on CROs, clinical trial sites, principal investigators and other third parties that may be less experienced with clinical trials or have different methods of performing such clinical trials than we are used to in the U.S.;
- · potential liability resulting from development work conducted by foreign distributors; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. Refer to "Business - Government Regulation - Regulation in China" for a discussion of the regulatory requirements that are applicable to our current and planned business activities in China. In recent years, the regulatory framework in China regarding the pharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes. For example, the Chinese government has implemented regulations that impact distribution of pharmaceutical products in China. These regulations generally require that at most two invoices may be issued throughout the distribution chain. Failure to comply with the "Two-Invoices" regulations would prevent us from accessing the market in China. As a result of the "Two-Invoices" regulation, we, rather than AstraZeneca, have been directly engaging distributors and a third-party logistics provider, and we are planning on modifying the distribution responsibilities under the China Agreement such that both companies will work together to manage the distribution network. FibroGen China Anemia Holdings, Ltd ("FibroGen China") has never managed distribution of pharmaceutical products, and this new distribution structure may impose higher costs or limit or delay our ability to sell products to our principal customers, and may limit the near term sales of our products. Any other such changes or amendments may result in increased compliance costs on our business or cause delays in or prevent the successful development or commercialization of our product candidates in China. Any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China.

We plan to use our own manufacturing facilities in China to produce roxadustat API and roxadustat drug product. As an organization, we have limited experience in the construction, licensure, and operation of a manufacturing plant, and accordingly we cannot assure you we will be able to meet regulatory requirements to operate our plant and to sell our products.

We have two manufacturing facilities in China, with one located in Beijing and the other in Cangzhou, Hebei. However, as an organization, we have limited experience licensing and operating commercial manufacturing facilities.

We will be obligated to comply with continuing cGMP requirements and there can be no assurance that we will maintain all of the appropriate licenses required to manufacture our product candidates for clinical and commercial use in China. In addition, we and our product suppliers must continually spend time, money and effort in production, record-keeping and quality assurance and appropriate controls in order to ensure that any products manufactured in our facilities meet applicable specifications and other requirements for product safety, efficacy and quality and there can be no assurance that our efforts will continue to be successful in meeting these requirements.

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Manufacturing facilities in China are subject to periodic unannounced inspections by the NMPA and other regulatory authorities. We expect to depend on these facilities for our product candidates and business operations in China. Natural disasters or other unanticipated catastrophic events, including power interruptions, water shortages, storms, fires, pandemics, earthquakes, terrorist attacks, government appropriation of our facilities, and wars, could significantly impair our ability to operate our manufacturing facilities. Certain equipment, records and other materials located in these facilities would be difficult to replace or would require substantial replacement lead time that would impact our ability to successfully commercialize our product candidates in China. The occurrence of any such event could materially and adversely affect our business, financial condition, results of operations, cash flows and prospects.

In addition to manufacturing, we are responsible for pharmacovigilance, medical affairs, and management of the third-party distribution logistics for roxadustat in China. We have no experience in these areas as a company, and accordingly we cannot assure you we will be able to meet regulatory requirements or operate in these capacities successfully.

We are responsible for commercial manufacturing, pharmacovigilance, medical affairs, and management of the third-party distribution logistics for roxadustat commercial activities in China. While we have been increasing our staffing in these areas, as a company, we have no experience managing or operating these functions for a commercial product and there can be no guarantee that we will do so efficiently or effectively. Mistakes or delays in these areas could limit our ability to successfully commercialize roxadustat in China, could limit our eventual market penetration, sales and profitability, and could subject us to significant liability in China.

Our business could be adversely affected by the effects of health epidemics in regions where we have significant manufacturing facilities, concentrations of customers, or other business operations. We have significant operations in China and depend on China manufacturing operations for various stages of our worldwide supply chain for roxadustat. We do not yet know the full extent of the impact on our roxadustat global supply chain or China operations from the disease caused by the 2019 novel coronavirus ("COVID-19"). In addition, if COVID-19 becomes a worldwide pandemic, it could materially affect our operations globally, including at our headquarters in San Francisco, California, and our clinical trials that are taking place predominantly in the U.S., Europe and China.

Our business could be adversely affected by health epidemics in regions where we have significant manufacturing facilities, concentrations of customers, or other business operations.

We have taken measures to minimize the health risks of COVID-19 as the safety and well-being of our staff is our top priority. While we have resumed manufacturing operations in China, we currently expect many of our employees to continue transitioning from working from home to returning to our offices following the closure of our offices in Beijing, Shanghai, and Canghzou in February 2020. Our collaboration partner AstraZeneca is also in the process of resuming operations. In addition, many governments, including the Chinese government, have taken measures to restrict travel to reduce the spread of COVID-19, which may limit our operational capabilities.

Due to these and potentially additional business disruptions, there may be delays to our roxadustat supply chain, problems with our distribution or warehousing vendors, or delays to our (and our partners') commercialization and launch activities in China (including efforts to list roxadustat in hospitals), all of which could have a material impact on our revenue.

If the COVID-19 outbreak continues to spread, particularly outside of China, we may need to limit operations again in China or implement limitations, including work from home policies, in the U.S. There is a risk that other countries or regions may be less effective at containing COVID-19, or it may be more difficult to contain if the outbreak reaches a larger population or broader geography, in which case the risks described herein could be elevated significantly.

In particular, while we and our Chinese manufacturing partner WuXi STA have resumed manufacturing operations, we only have a limited stockpile of roxadustat API and Drug Product, and therefore, if there is a greater impact from the COVID-19 outbreak than currently expected, or if operations are halted again, we could face shortages in our China and global supply chains.

In addition, current and upcoming clinical trials run in China by us and our partner AstraZeneca may be affected by the COVID-19 outbreak. Site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 outbreak, but the extent of these potential delays is unknown at this time. If COVID-19 becomes a worldwide pandemic, it may delay enrollment in our global clinical trials, including here in the U.S., and some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, which would delay our clinical results and ultimate commercialization of our product candidates affected.

The COVID-19 outbreak has already impacted China's economy and the global economy, and China's healthcare system as a whole has been disrupted since the beginning of 2020. It is unknown how long this disruption will continue and how it will affect the government healthcare budget and pharmaceutical sales as patient visits to hospitals and physician engagement and medical affairs efforts have been greatly affected due to the outbreak. The effect on the government budget in China could lead to increased pressure on drug prices which could affect future reimbursement or our ability to obtain hospital listings for roxadustat.

For roxadustat specifically, while the effect on our sales may be more limited than for more established drugs as we have only recently been added to the National Reimbursement Drug List and are still in the process of securing hospital listings, we do expect some delay in our launch-progress, including with respect to increasing sales and obtaining more hospital listings.

The ultimate impact of the COVID-19 outbreak is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, healthcare systems, or the global economy as a whole. However, these effects could have a material impact on our operations and revenue and we will continue to monitor the COVID-19 situation closely.

We and our collaboration partner in China, AstraZeneca, may experience difficulties in successfully generating sales of roxadustat in China.

We and AstraZeneca have a profit sharing arrangement with respect to roxadustat in China and any difficulties we may experience in generating sales will affect our bottom line. Difficulties may be related to our ability to maintain reasonable pricing and reimbursement, obtain hospital listing, or other difficulties related to distribution, marketing, and sales efforts in China. For example, our current National Reimbursement Drug List reimbursement pricing is effective for a standard two-year period (between January 1, 2020 to December 31, 2021), after which time we will have to renegotiate a new price for roxadustat, which may be lower. Sales of roxadustat in China may be limited due to the complex nature of the healthcare system, low average personal income, pricing controls, still developing infrastructure and potentially rapid competition from other products. The hospital listing process is critical to roxadustat's near-term commercial success in China and may take many years to obtain the majority of hospital listings.

The retail prices of any product candidates that we develop may be subject to control, including periodic downward adjustment, by Chinese government authorities.

The price for pharmaceutical products is highly regulated in China, both at the national and provincial level. Price controls may reduce prices to levels significantly below those that would prevail in less regulated markets or limit the volume of products that may be sold, either of which may have a material and adverse effect on potential revenues from sales of roxadustat in China. Moreover, the process and timing for the implementation of price restrictions is unpredictable, which may cause potential revenues from the sales of roxadustat to fluctuate from period to period.

If our planned business activities in China fall within a restricted category under the China Catalog for Guidance for Foreign Investment, we will need to operate in China through a variable interest entity ("VIE") structure.

The China Catalog for Guidance for Foreign Investment sets forth the industries and sectors that the Chinese government encourages and restricts with respect to foreign investment and participation. The Catalog for Guidance for Foreign Investment is subject to revision from time to time by the China Ministry of Commerce. While we currently do not believe the development and marketing of roxadustat falls within a restricted category under the Catalog for Guidance for Foreign Investment, if roxadustat does fall under such a restricted category, we will need to operate in China through a VIE structure. A VIE structure involves a wholly foreign-owned enterprise that would control and receive the economic benefits of a domestic Chinese company through various contractual relationships. Such a structure would subject us to a number of risks that may have an adverse effect on our business, including that the Chinese government may determine that such contractual arrangements do not comply with applicable regulations, Chinese tax authorities may require us to pay additional taxes, shareholders of our VIEs may have potential conflicts of interest with us, and we may lose the ability to use and enjoy assets held by our VIEs that are important to the operations of our business if such entities go bankrupt or become subject to dissolution or liquidation proceedings. VIE structures in China have come under increasing scrutiny from accounting firms and the Securities and Exchange Commission ("SEC") staff. If we do attempt to use a VIE structure and are unsuccessful in structuring it so as to qualify as a VIE, we would not be able to consolidate the financial statements of the VIE with our financial statements, which could have a material adverse effect on our operating results and financial condition.

FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.

We plan to conduct all of our business in China through FibroGen China and FibroGen Beijing. We may rely on dividends and royalties paid by FibroGen Beijing for a portion of our cash needs, including the funds necessary to service any debt we may incur and to pay our operating costs and expenses. The payment of dividends by FibroGen Beijing is subject to limitations. Regulations in China currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in China. FibroGen Beijing is not permitted to distribute any profits until losses from prior fiscal years have been recouped and in any event must maintain certain minimum capital requirements. FibroGen Beijing is also required to set aside at least 10.0% of its after-tax profit based on Chinese accounting standards each year to its statutory reserve fund until the cumulative amount of such reserves reaches 50.0% of its registered capital. Statutory reserves are not distributable as cash dividends. In addition, if FibroGen Beijing incurs debt on its own behalf in the future, the agreements governing such debt may restrict its ability to pay dividends or make other distributions to us. As of December 31, 2019, approximately \$7.0 million of our cash and cash equivalents is held in China.

Any capital contributions from us to FibroGen Beijing must be approved by the Ministry of Commerce in China, and failure to obtain such approval may materially and adversely affect the liquidity position of FibroGen Beijing.

The Ministry of Commerce in China or its local counterpart must approve the amount and use of any capital contributions from us to FibroGen Beijing, and there can be no assurance that we will be able to complete the necessary government registrations and obtain the necessary government approvals on a timely basis, or at all. If we fail to do so, we may not be able to contribute additional capital to fund our Chinese operations, and the liquidity and financial position of FibroGen Beijing may be materially and adversely affected.

We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.

Most of our product sales will occur in local Chinese currency and our operating results will be subject to volatility from currency exchange rate fluctuations. To date, we have not hedged against the risks associated with fluctuations in exchange rates and, therefore, exchange rate fluctuations could have an adverse impact on our future operating results. Changes in value of the Renminbi against the U.S. dollar, Euro and other currencies is affected by, among other things, changes in China's political and economic conditions. Currently, the Renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. Any significant currency exchange rate fluctuations may have a material adverse effect on our business and financial condition.

In addition, the Chinese government imposes controls on the convertibility of the Renminbi into foreign currencies and the remittance of foreign currency out of China for certain transactions. Shortages in the availability of foreign currency may restrict the ability of FibroGen Beijing to remit sufficient foreign currency to pay dividends or other payments to us, or otherwise satisfy their foreign currency-denominated obligations. Under existing Chinese foreign exchange regulations, payments of current account items, including profit distributions, interest payments and balance of trade, can be made in foreign currencies without prior approval from the State Administration of Foreign Exchange ("SAFE") by complying with certain procedural requirements. However, approval from SAFE or its local branch is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The Chinese government may also at its discretion restrict access in the future to foreign currencies for current account transactions. If the foreign exchange control system prevents us from obtaining sufficient foreign currency to satisfy our operational requirements, our liquidity and financial position may be materially and adversely affected.

Because FibroGen Beijing's funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen Beijing deposits its funds could adversely affect our business.

Banks and other financial institutions in China do not provide insurance for funds held on deposit. As a result, in the event of a bank failure, FibroGen Beijing may not have access to funds on deposit. Depending upon the amount of money FibroGen Beijing maintains in a bank that fails, its inability to have access to cash could materially impair its operations.

We may be subject to tax inefficiencies associated with our offshore corporate structure.

The tax regulations of the U.S. and other jurisdictions in which we operate are extremely complex and subject to change. New laws, new interpretations of existing laws, such as the Base Erosion Profit Shifting project initiated by the Organization for Economic Co-operation and Development, and any legislation proposed by the relevant taxing authorities, or limitations on our ability to structure our operations and intercompany transactions may lead to inefficient tax treatment of our revenue, profits, royalties, and distributions, if any are achieved.

In addition, we and our foreign subsidiaries have various intercompany transactions. We may not be able to obtain certain benefits under relevant tax treaties to avoid double taxation on certain transactions among our subsidiaries. If we are not able to avail ourselves to the tax treaties, we could be subject to additional taxes, which could adversely affect our financial condition and results of operations.

On December 22, 2017, the U.S. enacted the Tax Act that instituted fundamental changes to the taxation of multinational corporations. The Tax Act includes changes to the taxation of foreign earnings by implementing a dividend exemption system, expansion of the current anti-deferral rules, a minimum tax on low-taxed foreign earnings and new measures to deter base erosion. There have been developing interpretations of the provisions of the Tax Act, including changes and issuance of new U.S. Treasury regulations, administrative interpretations, or court decisions since its inception. As regulations and guidance evolve with respect to the Tax Act, we continue to examine the impact to our business, which could have a material adverse effect on our business, results of operations or financial condition.

Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.

We seek to protect the products and technology that we consider important to our business by pursuing patent applications in China and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. We note that the filing of a patent application does not mean that we will be granted a patent, or that any patent eventually granted will be as broad as requested in the patent application or will be sufficient to protect our technology. There are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications not to be granted, including known or unknown prior art, deficiencies in the patent application, or lack of originality of the technology. Furthermore, the terms of our patents are limited. The patents we hold and the patents that may be granted from our currently pending patent applications have, absent any patent term adjustment or extension, a twenty-year protection period starting from the date of application.

Intellectual property rights and confidentiality protections in China may not be as effective as those in the U.S. or other countries for many reasons, including lack of procedural rules for discovery and evidence, low damage awards, and lack of judicial independence. Implementation and enforcement of China intellectual property laws have historically been deficient and ineffective and may be hampered by corruption and local protectionism. Policing unauthorized use of proprietary technology is difficult and expensive, and we may need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability and validity of our proprietary rights or those of others. The experience and capabilities of China courts in handling intellectual property litigation varies and outcomes are unpredictable. An adverse determination in any such litigation could materially impair our intellectual property rights and may harm our business.

Uncertainties with respect to the China legal system could have a material adverse effect on us.

The legal system of China is a civil law system primarily based on written statutes. Unlike in a common law system, prior court decisions may be cited for reference but are not binding. Because the China legal system continues to rapidly evolve, the interpretations of many laws, regulations and rules are not always uniform and enforcement of these laws, regulations and rules involve uncertainties, which may limit legal protections available to us. Moreover, decision makers in the China judicial system have significant discretion in interpreting and implementing statutory and contractual terms, which may render it difficult for FibroGen Beijing to enforce the contracts it has entered into with our business partners, customers and suppliers. Different government departments may have different interpretations of certain laws and regulations, and licenses and permits issued or granted by one government authority may be revoked by a higher government authority at a later time. Navigating the uncertainty and change in the China legal system will require the devotion of significant resources and time, and there can be no assurance that our contractual and other rights will ultimately be enforced.

Changes in China's economic, political or social conditions or government policies could have a material adverse effect on our business and operations.

Chinese society and the Chinese economy continue to undergo significant change. Changes in the regulatory structure, regulations, and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy, but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the regulatory structure and structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes and structural changes, any of which could materially and adversely affect FibroGen Beijing's development and commercialization timelines, liquidity, access to capital, and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China. In addition, the changing government regulations and policies could result in delays and cost increases to our development, manufacturing, approval, and commercialization timelines in China.

Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may materially and adversely affect our business, financial condition and results of operations.

We are subject to China Labor Contract Law, which provides strong protections for employees and imposes many obligations on employers. The Labor Contract Law places certain restrictions on the circumstances under which employers may terminate labor contracts and require economic compensation to employees upon termination of employment, among other things. In addition, companies operating in China are generally required to contribute to labor union funds and the mandatory social insurance and housing funds. Any failure by us to comply with Chinese labor and social insurance laws may subject us to late fees, fines and penalties, or cause the suspension or termination of our ability to conduct business in China, any of which could have a material and adverse effect on business, results of operations and prospects.

Developments relating to the United Kingdom's referendum vote in favor of leaving the European Union could adversely affect us.

Effective January 31, 2020, the United Kingdom commenced an exit from the European Union, commonly referred to as "Brexit." During a transition period (set to expire on December 31, 2020), the British government will continue to negotiate the terms of the United Kingdom's future relationship with the European Union. The outcome of these negotiations is uncertain, and we do not know to what extent Brexit will ultimately impact the business and regulatory environment in the United Kingdom, the rest of Europe, or other countries. The effects of the United Kingdom's withdrawal from the European Union, and the perceptions as to its impact, are expected to be far-reaching and may adversely affect business activity and economic conditions in Europe and globally and could continue to contribute to instability in global financial markets, including foreign exchange markets. The United Kingdom's withdrawal from the European Union could also have the effect of disrupting the free movement of goods, services and people between the United Kingdom and Europe and could also lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which European laws to replace or replicate, including laws that could impact our ability, or our collaborator's ability in the case of roxadustat, to obtain approval of our products or sell our products in the United Kingdom. Changes impacting our ability to conduct business in the United Kingdom or other European countries, or changes to the regulatory regime applicable to our operations in those countries (such as with respect to the approval of our product candidates), may materially and adversely impact our business, prospects, operating results, and financial condition.

Risks Related to the Operation of Our Business

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, commercialization and administration capabilities or contract with third parties to provide these capabilities for us. As our operations expand and we continue to undertake the efforts and expense to operate as a public reporting company, we expect that we will need to increase the responsibilities on members of management in order to manage any future growth effectively. Our failure to accomplish any of these steps could prevent us from successfully implementing our strategy and maintaining the confidence of investors in us.

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Loss of senior management and key personnel, including the recent passing of our founder, chairman and chief executive officer, could adversely affect our ability to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.

We are highly dependent on members of our senior management team. In August 2019, Thomas B. Neff, our founder, chairman and chief executive officer, passed away, and subsequently James Schoeneck, a longtime member of our Board of Directors, was appointed as interim chief executive officer. On January 6, 2020, we announced the appointment of Enrique Conterno as chief executive officer, with Mr. Schoeneck stepping down from the interim role. The loss of Mr. Neff and his knowledge of the Company's programs may be disruptive to our operations and could negatively impact the development and commercialization of our product candidates, our existing collaborative relationships, and our ability to successfully implement our business strategy, as could changes in our executive team in the future.

Recruiting and retaining qualified commercial, development, scientific, clinical, and manufacturing personnel are and will continue to be critical to our success, particularly as we expand our commercialization operations. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

There is also significant competition, in particular in the San Francisco Bay Area, for the hiring of experienced and qualified personnel, which increases the importance of retention of our existing personnel. If we are unable to continue to attract and retain personnel with the quality and experience applicable to our product candidates, our ability to pursue our strategy will be limited and our business and operations would be adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing, manufacturing and commercialization of our product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under state consumer protection acts. If we are unable to obtain insurance coverage at levels that are appropriate to maintain our business and operations, or if we are unable to successfully defend ourselves against product liability claims, we may incur substantial liabilities or otherwise cease operations. Product liability claims may result in:

- termination of further development of unapproved product candidates or significantly reduced demand for any approved products;
- material costs and expenses to defend the related litigation;
- a diversion of time and resources across the entire organization, including our executive management;
- product recalls, withdrawals or labeling restrictions;
- termination of our collaboration relationships or disputes with our collaboration partners; and
- reputational damage negatively impacting our other product candidates in development.

If we fail to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, we may not be able to continue to develop our product candidates. We maintain product liability insurance in a customary amount for the stage of development of our product candidates. Although we believe that we have sufficient coverage based on the advice of our third-party advisors, there can be no assurance that such levels will be sufficient for our needs. Moreover, our insurance policies have various exclusions, and we may be in a dispute with our carrier as to the extent and nature of our coverage, including whether we are covered under the applicable product liability policy. If we are not able to ensure coverage or are required to pay substantial amounts to settle or otherwise contest the claims for product liability, our business and operations would be negatively affected.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, collaboration partners, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We upgraded our disaster and data recovery capabilities in 2017, however, to the extent that any disruption or security breach, in particular with our partners' operations, results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and it could result in a material disruption and delay of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

We depend on sophisticated information technology systems to operate our business and a cyber-attack or other breach of these systems could have a material adverse effect on our business.

We rely on information technology systems to process, transmit and store electronic information in our day-to-day operations. The size and complexity of our information technology systems makes them vulnerable to a cyber-attack, malicious intrusion, breakdown, destruction, loss of data privacy or other significant disruption. While we have recently upgraded our disaster data recovery program, a successful attack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyber-attacks are becoming more sophisticated and frequent. We have invested in our systems and the protection and recoverability of our data to reduce the risk of an intrusion or interruption, and we monitor and test our systems on an ongoing basis for any current or potential threats. There can be no assurance that these measures and efforts will prevent future interruptions or breakdowns. If we fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to these systems, we could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating costs and expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows.

Our headquarters are located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business, results of operations and financial condition.

We and some of the third-party service providers on which we depend for various support functions are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires.

We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, or otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place are unlikely to provide adequate protection in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above your purchase price.

In general, pharmaceutical, biotechnology and other life sciences company stocks have been highly volatile in the current market. The volatility of pharmaceutical, biotechnology and other life sciences company stocks is sometimes unrelated to the operating performance of particular companies and biotechnology and life science companies stocks often respond to trends and perceptions rather than financial performance. In particular, the market price of shares of our common stock could be subject to wide fluctuations in response to the following factors:

- results of clinical trials of our product candidates, including roxadustat and pamrevlumab;
- the timing of the release of results of and regulatory updates regarding our clinical trials;
- the level of expenses related to any of our product candidates or clinical development programs;
- results of clinical trials of our competitors' products;
- safety issues with respect to our product candidates or our competitors' products;
- regulatory actions with respect to our product candidates and any approved products or our competitors' products;
- fluctuations in our financial condition and operating results, which will be significantly affected by the manner in which we recognize revenue from the achievement of milestones under our collaboration agreements;
- adverse developments concerning our collaborations and our manufacturers;
- the termination of a collaboration or the inability to establish additional collaborations;
- the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- changes in legislation or other regulatory developments affecting our product candidates or our industry;
- fluctuations in the valuation of the biotechnology industry and particular companies perceived by investors to be comparable to us;
- speculation in the press or investment community;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- activities of the government of China, including those related to the pharmaceutical industry as well as industrial policy generally;
- performance of other U.S. publicly traded companies with significant operations in China;
- changes in market conditions for biopharmaceutical stocks; and
- the other factors described in this "Risk Factors" section.

As a result of fluctuations caused by these and other factors, comparisons of our operating results across different periods may not be accurate indicators of our future performance. Any fluctuations that we report in the future may differ from the expectations of market analysts and investors, which could cause the price of our common stock to fluctuate significantly. Moreover, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources and could also require us to make substantial payments to satisfy judgments or to settle litigation.

If securities or industry analysts do not continue to publish research or reports about our business, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

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Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.

As of January 31, 2020, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 27.60% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date and shares issuable upon settlement of restricted stock units that will vest within 60 days after such date. This percentage is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G, if any, filed with the SEC, which information may not be accurate as of January 31, 2020. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. The interests of this group may differ from those of other stockholders and they may vote their shares in a way that is contrary to the way other stockholders vote their shares. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our business, results of operations, financial condition and cash flows and future prospects.

While we currently have no specific plans to acquire any other businesses, we may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our present or future product candidates and business or otherwise offer opportunities for us. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our existing stockholders' percentage of ownership;
- · incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products or technologies, or employees or other assets of the acquisition target;
- increases to our expenses;
- disclosed or undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- reprioritization of our development programs and even cessation of development and commercialization of our current product candidates;
- harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current directors or management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a
 majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed prior to the end of their term only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a
 quorum;
- require a supermajority vote of the holders of our common stock or the majority vote of our board of directors to amend our bylaws;
- require a supermajority vote of the holders of our common stock to amend the classification of our board of directors into three classes and to amend certain other provisions of our certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Moreover, because we are incorporated in Delaware, we are governed by certain anti-takeover provisions under Delaware law which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. We are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Changes in our tax provision or exposure to additional tax liabilities could adversely affect our earnings and financial condition.

As a multinational corporation, we are subject to income taxes in the U.S. and various foreign jurisdictions. Significant judgment is required in determining our global provision for income taxes and other tax liabilities. In the ordinary course of a global business, there are intercompany transactions and calculations where the ultimate tax determination is uncertain. Our income tax returns are subject to audits by tax authorities. Although we regularly assess the likelihood of adverse outcomes resulting from these examinations to determine our tax estimates, a final determination of tax audits or tax disputes could have an adverse effect on our results of operations and financial condition.

We are also subject to non-income taxes, such as payroll, sales, use, value-added, net worth, property, gross receipts, and goods and services taxes in the U.S., state and local, and various foreign jurisdictions. We are subject to audit and assessments by tax authorities with respect to these non-income taxes and may have exposure to additional non-income tax liabilities, which could have an adverse effect on our results of operations and financial condition.

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In addition, our judgment in providing for the possible impact of the Tax Act remains subject to developing interpretations of the provisions of the Tax Act. As regulations and guidance evolve with respect to the Tax Act, we continue to examine the impact to our tax provision or exposure to additional tax liabilities, which could have a material adverse effect on our business, results of operations or financial condition.

Tariffs imposed by the U.S. and those imposed in response by other countries, as well as rapidly changing trade relations, could have a material adverse effect on our business and results of operations.

Changes in U.S. and foreign governments' trade policies have resulted in, and may continue to result in, tariffs on imports into and exports from the U.S. Throughout 2018 and 2019, the U.S. imposed tariffs on imports from several countries, including China. In response, China has proposed and implemented their own tariffs on certain products, which may impact our supply chain and our costs of doing business. If we are impacted by the changing trade relations between the U.S. and China, our business and results of operations may be negatively impacted. Continued diminished trade relations between the U.S. and other countries, including potential reductions in trade with China and others, as well as the continued escalation of tariffs, could have a material adverse effect on our financial performance and results of operations.

Our amended and restated certificate of incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in our product candidates and maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our corporate and research and development operations are located in San Francisco, California, where we lease approximately 234,000 square feet of office and laboratory space with approximately 35,000 square feet subleased. The lease for our San Francisco headquarters expires in 2023. We also lease approximately 67,000 square feet of office and manufacturing space in Beijing, China. Our lease in China expires in 2021. We have constructed a commercial manufacturing facility of approximately 5,500 square meters in Cangzhou, China, on approximately 33,000 square meters of land. Our right to use such land expires in 2068. We believe our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

ITEM 3. LEGAL PROCEEEDINGS

We are not currently a party to any material legal proceedings.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

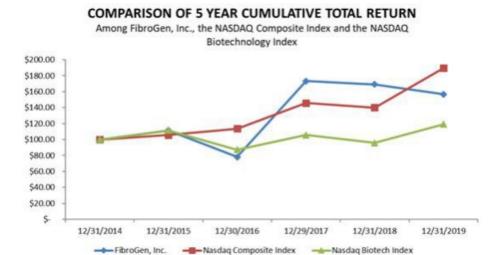
ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY **SECURITIES**

Market Information for Common Stock

Our common stock has been listed on the NASDAQ Global Select Market ("NASDAQ") since November 14, 2014, under the symbol "FGEN." Prior to our initial public offering, there was no public market for our common stock.

Stock Price Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock since December 31, 2014 to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of \$100 on December 31, 2014, in our common stock, the stocks comprising the NASDAQ Composite Index, and the stocks comprising the NASDAQ Biotechnology Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.



The above Stock Price Performance Graph and related information shall not be deemed "soliciting material" or to be "filed" with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act or Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

-----Nasdag Biotech Index

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Stockholders

As of January 31, 2020, there were 136 registered stockholders of record for our common stock. This number of registered stockholders does not include stockholders whose shares are held in street name by brokers and other nominees, or may be held in trust by other entities. Therefore, the actual number of stockholders is greater than this number of registered stockholders of record.

Use of Proceeds from Initial Public Offering of Common Stock

On November 13, 2014, our Registration Statement on Form S-1, as amended (Reg. Nos. 333-199069 and 333-200189) was declared effective in connection with the initial public offering of our common stock. There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on November 14, 2014.

Recent Sales of Unregistered Securities

During the year ended December 31, 2019, a warrant to purchase 4,430 shares of our common stock was exercised at a per share price of \$15.00.

These shares issued pursuant to the warrant were not registered under the Securities Act of 1933, as amended, in reliance upon the exemption set forth in Section 4(a)(2) of such Act for transactions not involving a public offering.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. SELECTED FINANCIAL DATA

The selected consolidated results of operations data for the years ended December 31, 2019, 2018 and 2017, and the consolidated balance sheet data as of December 31, 2019 and 2018 should be read together with Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations" and in conjunction with the consolidated financial statements, related notes, and other financial information included elsewhere in this Annual Report. The selected consolidated results of operations data for the year ended December 31, 2016 and 2015 and the consolidated balance sheet data as of December 31, 2017, 2016 and 2015 have been derived from audited financial statements not included herein. Our historical results are not necessarily indicative of the results to be expected in the future.

	Years Ended December 31,									
	2019			2018		2017		2016		2015
				(in thousar	ıds, (except for per s	hare	data)		
Result of Operations										
Revenue:										
License revenue	\$	177,086	\$	22,269	\$	9,933	\$	50,607	\$	89,401
Development and other revenue		114,115		125,913		121,063		132,582		82,985
Product revenue		(34,624)		64,776		-				-
Total revenue		256,577		212,958		130,996		183,189		172,386
Operating expenses:										
Cost of goods sold		1,147		-		-		-		-
Research and development		209,265		235,839		196,517		187,206		214,089
Selling, general and administrative		135,479		63,812		51,760		46,025		44,364
Total operating expenses	· ·	345,891		299,651		248,277		233,231		258,453
Net loss	\$	(76,970)	\$	(86,420)	\$	(120,875)	\$	(58,068)	\$	(94,221)
Net loss per share - basic and diluted	\$	(0.89)	\$	(1.03)	\$	(1.66)	\$	(0.93)	\$	(1.56)
					D	ecember 31,				
		2019		2018	2017		2016			2015
						(in thousands)				
Balance Sheet Data:										
Cash and cash equivalents	\$	126,266	\$	89,258	\$	673,658	\$	173,782	\$	153,324
Short-term and long-term investments		468,609		587,964		72,566		150,407		159,567
Working capital		599,745		600,982		663,010		192,806		131,468
Total assets		857,397		880,598		898,650		469,552		470,574
Deferred revenue		99,939		149,880		154,911		154,737		141,511
Accumulated deficit		(784,720)		(715,827)		(630,657)		(509,782)		(451,714)
Total stockholders' equity		516,135		509,199		528,467		115,798		133,902
			84							

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes and other financial information included in Item 15 of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business, international operations and product candidates, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" section of this Annual Report for a discussion of important factors that could cause our actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

BUSINESS OVERVIEW

We were incorporated in 1993 in Delaware and are headquartered in San Francisco, California, with subsidiary offices in Beijing and Shanghai, People's Republic of China ("China"). We are a leading biopharmaceutical company developing and commercializing a pipeline of first-in-class therapeutics. We apply our pioneering expertise in hypoxia-inducible factor ("HIF"), connective tissue growth factor ("CTGF") biology, and clinical development to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer. Roxadustat, our most advanced product, is an oral small molecule inhibitor of HIF prolyl hydroxylase ("HIF-PH") activity that has received marketing authorization in China for the treatment of anemia caused by chronic kidney disease ("CKD") in dialysis and non-dialysis patients. In September 2019, roxadustat (Evrenzo®) was approved in Japan for the treatment of anemia associated with CKD in dialysis-dependent patients. In January 2020, Astellas Pharma Inc. ("Astellas") submitted a supplemental New Drug Application ("NDA") in Japan for the treatment of anemia in non-dialysis CKD patients. Our NDA filing for roxadustat for the treatment of anemia patients with dialysis-dependent CKD and non-dialysis-dependent CKD was accepted for review by the United States ("U.S.") Food and Drug Administration ("FDA") in February 2020, and Astellas is in the process of preparing a Marketing Authorization Application ("MAA") for submission to the European Medicines Agency ("EMA") in the second quarter of 2020 for the same indications. Roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes ("MDS"). Roxadustat is in Phase 2 clinical development for chemotherapy-induced anemia. Pamrevlumab, an anti-CTGF human monoclonal antibody, is in Phase 3 clinical development for the treatment of both idiopathic pulmonary fibrosis ("IPF") and pancreatic cancer. Pamrevlumab is also currently in a Phase 2 trial for Duch

Financial Highlights

		Years Ended December 31,							
	2019			2018	2017				
		(in thousands, except for per share data)							
Result of Operations									
Revenue	\$	256,577	\$	212,958	\$	130,996			
Operating costs and expenses		345,891		299,651		248,277			
Net loss		(76,970)		(86,420)		(120,875)			
Net loss per share - basic and diluted	\$	(0.89)	\$	(1.03)	\$	(1.66)			
			December 31, 2019		December 31, 2018				
				(in thousands)					
Balance Sheet									
Cash and cash equivalents			\$	126,266	\$	89,258			
Short-term and long-term investments			\$	468,609	\$	587,964			
Accounts receivable			\$	28,455	\$	63,684			

Our revenue for the year ended December 31, 2019 included the revenues recognized related to the following:

- Two regulatory milestones totaling \$130.0 million associated with the planned MAA submission to the EMA under the collaboration agreement with Astellas for roxadustat as a treatment for dialysis and non-dialysis CKD patients;
- A \$50.0 million regulatory milestone associated with the NDA submission to the FDA under the collaboration agreement with AstraZeneca for roxadustat as a treatment for dialysis and non-dialysis CKD patients;
- Three regulatory milestones totaling \$22.0 million associated with roxadustat being included on the updated National Reimbursement Drug List
 ("NRDL") released by China's National Healthcare Security Administration ("NHSA"); and
- A regulatory milestone of \$12.5 million associated with the NDA approval in Japan.

Meanwhile, our overall revenue for the year ended December 31, 2019 was reduced by \$36.3 million of a change in estimated variable consideration related to the API product revenue that was recognized in 2018 discussed below, which reflected the total difference between estimated and actual listed price and yield from the manufacture of bulk product tablets.

As comparison, our revenue for the year ended December 31, 2018 included the revenues recognized related to the following:

- A \$64.8 million product revenue for API delivered during 2018, under the amendment to the collaboration agreement with Astellas for roxadustat for the treatment of anemia in Japan ("Japan Agreement"), to conduct commercial scale manufacturing validation for roxadustat drug product in anticipation of commercial launch in Japan;
- A regulatory milestone of \$15.0 million associated with an NDA submission during 2018 in Japan;
- A \$6.0 million milestone under the collaboration agreements with AstraZeneca upon our receipt of marketing authorization from the NMPA for
 roxadustat, a first-in-class HIF-PH inhibitor, for the treatment of anemia caused by CKD in patients on dialysis; and
- A \$6.0 million milestone payable under the collaboration agreement with AstraZeneca upon our receipt of First Manufacturing Approval for a
 Product in the Field in the Territory, which allows production for Phase 4 clinical studies, patients' early experience programs, donation
 programs, as well as to supply products for testing and assessments required prior to launch.

Operating expenses increased for the year ended December 31, 2019 compared to the prior year primarily due to the following:

- · Higher outside service expenses related to co-promotional activities and scientific contract expenses;
- · Higher stock-based compensation related to the cumulative impact of stock option grant activities;
- Amortization of finance lease ROU assets and higher depreciation expenses related to the adoption of lease accounting guidance under ASC 842:
- · Higher legal expenses mainly associated with patent-related and international activities; and
- · Higher employee-related expenses resulting from higher average compensation level.

The increases were partially offset by:

- · Lower clinical trial expenses related to lower activities for roxadustat offset by higher activities for pamrevlumab; and
- Lower drug development expenses associated with drug substance manufacturing activities related to pamrevlumab, and capitalization of
 inventory manufacturing costs.

Our research and development expenses were \$209.3 million, \$235.8 million and \$196.5 million for the years ended December 31, 2019, 2018 and 2017, respectively. Since inception and through December 31, 2019, we have incurred a total of approximately \$2 billion in research and development expenses, a majority of which relates to the development of roxadustat, pamrevlumab and other HIF-PH inhibitors. We expect to continue to incur significant expenses and operating losses over at least the next several years and we expect our research and development expenses to increase in the future as we advance our product candidates through clinical trials and expand our product candidate portfolio. In addition, we expect to incur significant expenses relating to seeking regulatory approval for our product candidates and commercializing those products in various markets, including China. We consider the active management and development of our clinical pipeline to be particularly crucial to our long-term success. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming.

The actual probability of success for each of our product candidates and clinical programs, and our ability to generate product revenue and become profitable, depends upon a variety of factors, including the quality of the product candidate, clinical results, investment in the program, competition, manufacturing capability, commercial viability, and our and our partners' ability to successfully execute our development and commercialization plans. For a description of the numerous risks and uncertainties associated with product development, refer to "Risk Factors."

During the year ended December 31, 2019, we had a net loss of \$77.0 million, or net loss per basic and diluted share of \$0.89, as compared to a net loss of \$86.4 million, or net loss per basic and diluted share of \$1.03 for the prior year, primarily due to an increase in revenue, partially offset by an increase in operating expenses.

Cash and cash equivalents, investments and accounts receivable totaled \$623.3 million at December 31, 2019, a decrease of \$117.6 million from December 31, 2018, primarily due to cash used in operations.

Programs

Roxadustat, our most advanced product, is an oral small molecule inhibitor of HIF-PH activity that has received marketing authorization in China for the treatment of anemia caused by CKD in non-dialysis-dependent patients (adding the non-dialysis indication to the label for dialysis-dependent patients, which was approved in December 2018). In September 2019, roxadustat (Evrenzo®) was approved in Japan for the treatment of anemia associated with CKD in dialysis-dependent patients. In January 2020, Astellas submitted a supplemental NDA in Japan for the treatment of anemia in non-dialysis CKD patients. Our U.S. NDA filing for roxadustat for the treatment of anemia patients with dialysis-dependent CKD and non-dialysis-dependent CKD was accepted for review by the FDA in February 2020, and Astellas is in the process of preparing an MAA for submission to the EMA in the second quarter of 2020 for the same indications. Roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with MDS. Roxadustat is in Phase 2 clinical development for chemotherapy-induced anemia.

Pamrevlumab, an anti-CTGF human monoclonal antibody, is in Phase 3 clinical development for the treatment of both IPF and pancreatic cancer. Pamrevlumab is also currently in a Phase 2 trial for DMD.

Collaboration Partnerships for Roxadustat

Our current and future research, development, manufacturing and commercialization efforts with respect to roxadustat and our other product candidates currently in development depend on funds from our collaboration agreements with Astellas and AstraZeneca as described below.

Astellas

In June 2005, we entered into a collaboration agreement with Astellas for the development and commercialization (but not manufacture) of roxadustat for the treatment of anemia in Japan ("Japan Agreement"). In April 2006, we entered into the Europe Agreement with Astellas for roxadustat for the treatment of anemia in Europe, the Commonwealth of Independent States, the Middle East, and South Africa. Under these agreements, we provide Astellas the right to develop and commercialize roxadustat for anemia indications in these territories.

We share responsibility with Astellas for clinical development activities required for the U.S. and the Europe regulatory approval of roxadustat and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will own and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

The Astellas agreements will continue in effect until terminated. Either party may terminate the agreements for certain material breaches by the other party. In addition, Astellas will have the right to terminate the agreements for certain specified technical product failures, upon generic sales reaching a particular threshold, upon certain regulatory actions, or upon our entering into a settlement admitting the invalidity or unenforceability of our licensed patents. Astellas may also terminate the agreements for convenience upon advance written notice to us. In the event of any termination of the agreements, Astellas will transfer and assign to us the regulatory filings for roxadustat and will assign or license to us the relevant trademarks used with the products in the Astellas territories. Under certain terminations, Astellas is also obligated to pay us a termination fee

Consideration under these agreements includes a total of \$360.1 million in upfront and non-contingent payments, and milestone payments totaling \$557.5 million, of which \$542.5 million are development and regulatory milestones and \$15.0 million are commercial-based milestones. Total consideration, excluding development cost reimbursement and product sales-related payments, could reach \$917.6 million. The aggregate amount of such consideration received, through December 31, 2019 totals \$500.1 million. Additionally, under these agreements, Astellas pays 100% of the commercialization costs in its territories. Astellas will pay FibroGen a transfer price, based on net sales, in the low 20% range for our manufacture and delivery of roxadustat.

In September 2019, Japan's Ministry of Health, Labour and Welfare approved roxadustat for the treatment of anemia associated with dialysis CKD patients. Accordingly, the consideration of \$12.5 million associated with this milestone was included in the transaction price and allocated to performance obligations under the Japan Agreement in the third quarter of 2019. This milestone payment was received in October 2019.

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During the second quarter of 2019, we received positive topline results from analyses of pooled major adverse cardiac event ("MACE") and MACE+ data from its Phase 3 trials evaluating roxadustat as a treatment for dialysis and non-dialysis CKD patients, enabling Astellas to prepare for an MAA submission to the EMA in the second quarter of 2020, following our NDA submission to the FDA in 2019 and acceptance for review in February 2020. We evaluated the two regulatory milestone payments associated with the planned MAA submission and concluded that these milestones became probable of being achieved in the second quarter of 2019. Accordingly, the total consideration of \$130.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the Europe Agreement in the second quarter of 2019.

During the second quarter of 2018, Astellas reported positive results from the final Phase 3 CKD-dialysis trial of roxadustat in Japan, indicating that Astellas was ready to make an NDA submission for the treatment of anemia with roxadustat in CKD-dialysis patients in 2018. We evaluated the regulatory milestone payment associated with NDA submission in Japan based on variable consideration requirements under the current revenue standards and concluded that this milestone became probable of being achieved in the second quarter of 2018. Accordingly, the consideration of \$15.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the Japan Agreement, substantially all of which was recognized as revenue in 2018.

On November 30, 2018, FibroGen and Astellas entered into an amendment to the Japan Agreement that will allow Astellas to manufacture roxadustat drug product for commercialization in Japan (the "Japan Amendment"). Under this amendment, FibroGen would continue to manufacture and deliver to Astellas roxadustat API. The commercial terms of the Japan Agreement relating to the transfer price for roxadustat for commercial use remain substantially the same, reflecting an adjustment for the manufacture of drug product by Astellas rather than FibroGen. This amendment obligated Astellas to purchase a total of \$64.7 million API from FibroGen, all of which was delivered to Astellas in 2018. In 2019, a change in estimated variable consideration resulted in a \$36.3 million reduction to revenue, at the time the listed price for roxadustat was issued by the Japanese Ministry of Health, Labour and Welfare, which reflected the total difference between estimated and actual listed price and yield from the manufacture of bulk product tablets.

In the fourth quarter of 2018, we were engaged in the final stages of review with our partners over the proposed development of roxadustat for the treatment of chemotherapy-induced anemia. AstraZeneca and Astellas approved the program in December 2018 and January 2019, respectively. Costs associated with the development of this indication are shared 50-50 between our two partners. For revenue recognition purposes, we concluded that this new indication represents a modification to the Europe agreements and will be accounted for separately, meaning the development costs associated with the new indications are distinct from the original development costs. The development service period for roxadustat for the treatment of CIA under the Europe Agreement is estimated to continue through the end of 2023 to allow for development of this indication.

In addition, as of December 31, 2019, Astellas had separate investments of \$80.5 million in the equity of FibroGen, Inc.

AstraZeneca

In July 2013, we entered into the U.S./RoW Agreement a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in the U.S. and all territories not previously licensed to Astellas, except China. In July 2013, through our China subsidiary and related affiliates, we entered into the China Agreement a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in China. Under these agreements we provide AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories. We share responsibility with AstraZeneca for clinical development activities required for U.S. regulatory approval of roxadustat.

In 2015, we reached the \$116.5 million cap on our initial funding obligations (during which time we shared 50% of the joint initial development costs), therefore all development and commercialization costs for roxadustat for the treatment of anemia in CKD in the U.S., Europe, Japan and all other markets outside of China have been paid by Astellas and AstraZeneca since reaching the cap.

In China, FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") will conduct the development work for CKD anemia, will hold all of the regulatory licenses issued by China regulatory authorities, and will be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is also responsible for 100% of development expenses in all other licensed territories outside of China. We are responsible, through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the AstraZeneca agreements.

Under the AstraZeneca agreements, we will receive upfront and subsequent non-contingent payments totaling \$402.2 million. Potential milestone payments under the agreements total \$1.2 billion, of which \$571.0 million are development and regulatory milestones and \$652.5 million are commercial-based milestones. Total consideration under the agreements, excluding development cost reimbursement, transfer price payments, royalties and profit share, could reach \$1.6 billion. The aggregate amount of such consideration received through December 31, 2019 totals \$444.2 million.

Under the U.S./RoW Agreement, AstraZeneca will pay for all commercialization costs in the U.S. and RoW and AstraZeneca will be responsible for the U.S. commercialization of roxadustat, with FibroGen undertaking specified promotional activities in the end stage renal disease segment in the U.S. In addition, we will receive a transfer price for delivery of commercial product based on a percentage of net sales in the low- to mid-single digit range and AstraZeneca will pay us a tiered royalty on net sales of roxadustat in the low 20% range.

Under the China Agreement, which is conducted through FibroGen China Anemia Holdings, Ltd. ("FibroGen China"), the commercial collaboration is structured as a 50/50 profit share. AstraZeneca will conduct sales and marketing activities in China and fund roxadustat launch costs in China until FibroGen Beijing has achieved profitability. At that time, AstraZeneca will recoup 50% of their historical launch costs out of initial roxadustat profits in China. As of December 31, 2019, we accrued \$53.1 million of co-promotional expenses related to the estimated amount payable to AstraZeneca for such sales and marketing efforts. The payment for such amount is not expected to occur within the next year.

Payments under these agreements include over \$500.0 million in upfront, non-contingent and other payments received or expected to be received prior to the first U.S. approval, excluding development expense reimbursement.

AstraZeneca may terminate the U.S./RoW Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon 180 days prior written notice at will. If AstraZeneca terminates the U.S./RoW Agreement at will, in addition to any unpaid non-contingent payments, it will be responsible for paying for a substantial portion of the post-termination development costs under the agreed development plan until regulatory approval.

AstraZeneca may terminate the China Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon advance prior written notice at will. If AstraZeneca terminates our China Agreement at will, it will be responsible for paying for transition costs as well as make a specified payment to FibroGen China.

In the event of any termination of the agreements, but subject to modification upon termination for technical product failure, AstraZeneca will transfer and assign to us any regulatory filings and approvals for roxadustat in the affected territories that they may hold under our agreements, grant us licenses and conduct certain transition activities.

In December 2019, roxadustat has been included on the updated NRDL released by China's NHSA for the treatment of anemia in CKD, covering patients who are non-dialysis-dependent as well as those who are dialysis-dependent. The inclusion on the NRDL triggered a total of \$22.0 million milestones payable to us by AstraZeneca. Accordingly, the total consideration of \$22.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the U.S./ RoW Agreement in the fourth quarter of 2019.

As mentioned above, during the second quarter of 2019, we received positive topline results from analyses of pooled MACE and MACE+ data from its Phase 3 trials for roxadustat, enabling our U.S. NDA submission to the FDA. We evaluated the regulatory milestone payment associated with this NDA submission and concluded that this milestone became probable of being achieved in the second quarter of 2019. Accordingly, the consideration of \$50.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the U.S./ RoW Agreement in the second quarter of 2019. We submitted our NDA to the FDA in December 2019, which was accepted for review in February 2020.

On December 17, 2018, FibroGen Beijing, received marketing authorization from the NMPA for roxadustat, a first-in-class HIF-PH inhibitor, for the treatment of anemia caused by CKD in patients on dialysis. This approval triggered a \$6.0 million milestone payable to us by AstraZeneca. On December 29, 2018, FibroGen Beijing received First Manufacturing Approval for a Product in the Field in the Territory, which allows production for Phase 4 clinical studies, patients' early experience programs, donation programs, as well as to supply products for testing and assessments required prior to launch. This approval triggered a \$6.0 million milestone payable to us by AstraZeneca.

As mentioned above, in the fourth quarter of 2018, we were engaged in the final stages of review with our partners over the proposed development of roxadustat for the treatment of CIA. AstraZeneca and Astellas approved the program in December 2018 and January 2019, respectively. Costs associated with the development of this indication are expected to be shared 50-50 between our two partners. In addition to CIA, in December 2018, anemia of chronic inflammation ("ACI") and multiple myeloma ("MM") have been approved for development by AstraZeneca and is expected to be fully funded by them. For revenue recognition purposes, we concluded that the approval of additional research and development services for these new indications represent modifications to our collaboration agreements in the periods in which approval was received. The research and development services associated with the new indications are distinct from other promises in our collaboration agreements, and will be accounted for separately. The development service period for roxadustat for the treatment of CIA, ACI and MM under the AstraZeneca agreements is estimated to continue through the end of 2024, to allow for development of these additional indications.

Exhibit 31.1

CERTIFICATION

- I, Enrique Conterno, certify that;
- 1. I have reviewed this annual report on Form 10-K of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in the Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 2, 2020

/s/ Enrique Conterno
Enrique Conterno
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

- I, Pat Cotroneo, certify that;
- 1. I have reviewed this annual report on Form 10-K of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in the Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 2, 2020

/s/ Pat Cotroneo

Pat Cotroneo
Senior Vice President, Finance and Chief Financial
Officer (Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Enrique Conterno, Chief Executive Officer of FibroGen, Inc. (the "Company"), and Pat Cotroneo, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

- 1. The Company's Annual Report on Form 10-K for the year ended December 31, 2019 (the "Annual Report"), to which this Certification is attached as Exhibit 32.1, fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and
- 2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of the 2nd day of March, 2020.

/s/ Enrique Conterno
Enrique Conterno
Chief Executive Officer

/s/ Pat Cotroneo
Pat Cotroneo
Senior Vice President, Finance and Chief Financial Officer

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of FibroGen, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

EXHIBIT X

S&P Global Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN FQ1 2020 Earnings Call Transcripts

Thursday, May 07, 2020 9:00 PM GMT

S&P Global Market Intelligence Estimates

	-FQ1 2020-			-FQ2 2020-	-FY 2020-	-FY 2021-
	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS	CONSENSUS	CONSENSUS
EPS Normalized	(0.48)	(0.89)	NM	(0.36)	(0.93)	(1.09)
Revenue (mm)	72.58	24.40	▼ (66.38 %)	66.85	330.80	376.87

Currency: USD

Consensus as of May-05-2020 9:45 PM GMT

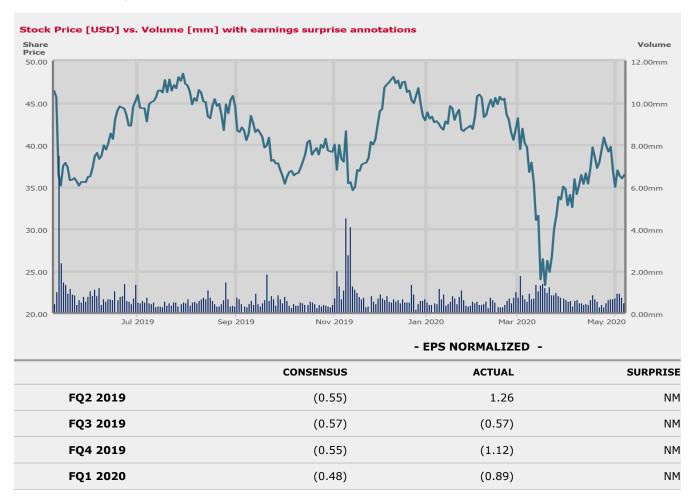


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EXECUTIVES

Christine L. Chung Senior Vice President of China Operations

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Enrique A. Conterno

CEO & Director

K. Peony Yu

Chief Medical Officer

Michael Tung

Investor Relations Executive

Pat Cotroneo

Senior VP of Finance & CFO

ANALYSTS

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Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Kyuwon Choi

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Michael Jonathan Yee

Jefferies LLC, Research Division

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Presentation

Operator

Ladies and gentlemen, thank you for standing by, and welcome to the FibroGen First Quarter 2020 Financial Results. [Operator Instructions] Please be advised that today's conference is being recorded. [Operator Instructions]

I would now like to hand the conference over to your speaker today, Mr. Michael Tung. Please go ahead, sir.

Michael Tung

Investor Relations Executive

Thank you, operator, and good afternoon, everyone. Thank you for joining us on today's call to discuss FibroGen's results for the first quarter of 2020. Today's call will be led by Enrique Conterno, our Chief Executive Officer. Enrique will be joined by Dr. Peony Yu, our Chief Medical Officer; Ms. Chris Chung, our Senior Vice President of China Operations; Dr. Elias Kouchakji, our Senior Vice President of Clinical Development, Drug Safety and Pharmacovigilance; and Mr. Pat Cotroneo, our Chief Financial Officer.

Before we begin, I would like to point out that we may make forward-looking statements regarding our business, including our collaborations with AstraZeneca and Astellas; financial guidance; the initiation, enrollment, design, conduct and results of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities; commercial results and results of operations; risks related to our business; and certain other business matters.

For risks and uncertainties regarding our business and statements made on the call today as well as factors beyond our control that may cause differences between current expectations and actual results, we refer you to our annual report on Form 10-K for the fiscal year ended December 31, 2019, and to our quarterly report on Form 10-Q for the quarter ended March 31, 2020, filed with the Securities and Exchange Commission. Copies of these filings can be found in the Investors section of our website.

We undertake no obligation to update any forward-looking statement, whether as a result of new information, future development or otherwise. The format for today's call includes prepared remarks from FibroGen's management team, and then we'll open the lines to take your questions. The press release reporting our financial results and business update and the webcast for today's conference call can be found on the Investors section of FibroGen's website at www.fibrogen.com.

And now I would like to turn the call over to Enrique Conterno, our CEO. Enrique?

Enrique A. Conterno

CEO & Director

Thank you, Mike. Good afternoon, everyone, and welcome to our first quarter 2020 earnings call. Given the challenges presented by the COVID-19 pandemic, I would like to take a moment on behalf of FibroGen to reassure patients, health care providers, investigators and stakeholders of our continued commitment to bring to patients our potential, first-in-class medicine for the treatment of chronic and life-threatening conditions. Governments, businesses and society in general, have taken unprecedented measures to mitigate the spread of the COVID-19 outbreak.

Like many businesses, FibroGen has taken a number of actions to support both our workforce and communities in these challenging times. In the U.S., our employees are working remotely when possible. While in China, they are now back working in our offices, manufacturing plants and the field. We have implemented protocols globally to minimize the risk of illness for our employees who need to work on-site at any of our facilities.

Despite the difficult circumstances, we remain committed to ensuring the regulatory and commercial success of roxadustat, a potentially transformational oral medicine in anemia therapy first demonstrated in patients with chronic kidney disease.

With pamrevlumab, we are implementing a comprehensive plan to accelerate development across the 3 indications of idiopathic pulmonary fibrosis, or IPF, locally advanced unresectable pancreatic cancer, or LAPC, and Duchenne muscular dystrophy or DMD once the situation with COVID-19 improves.

Finally, we continue to advance the innovation of our hypoxia-inducible factor, or HIF, and connective tissue growth factor, or CTGF, platforms.

Our business continuity plans are in effect, and we're seeing an impact to our operations resulting from COVID-19, we remain confident that FibroGen has the resources and capabilities to navigate through these uncertain times and achieve our stated goals.

As China comes back online, we are continuing our manufacturing operations and launch efforts there. We have ample drug supply to support both the roxadustat launches and clinical trials in additional indications as well as the pamrevlumab clinical trials.

We will continue to monitor the situation closely. To our employees and patients and to the thought leaders, clinicians, regulators and countless others who interact with FibroGen, please know our thoughts are with you, and your families.

Now let me begin with roxadustat. During the first quarter, our roxadustat NDA submission was accepted by the FDA, and interaction with the FDA on the file continues. We expect action by the PDUFA date of December 20, 2020.

In Europe, the Marketing Authorization Application filing for roxadustat for the treatment of anemia in both dialysis- and non-dialysis-dependent patients with CKD is expected in the second quarter of 2020. We and our partners are working diligently in preparation to make this novel, first-in-class medicine available to as many patients worldwide as quickly as possible.

Turning to China. As you know, roxadustat was first approved in China and was included in the National Drug Reimbursement List, or NRDL, which went into effect at the beginning of the year. A key focus has been and continues to be expanding hospital listing so that roxadustat can be widely prescribed. We saw positive momentum in hospital listings in January before the start of the COVID-19 restrictions, which caused a slowdown in new listings from late January to late March. As we stand here today, we have seen a steady return to a new normal in China, and we continue to be encouraged by the roxadustat opportunity there.

The COVID-19 pandemic, however, is still causing disruption in clinical trials across the globe. And the FDA, EMA and other regulatory agencies have issued guidance for the conducts of clinical trials during the pandemic. We are incorporating these regulatory recommendations as appropriate are closed on clinical trials.

Our first priority at FibroGen is ensuring the safety and well-being of the patients participating in our studies.

While we do not intend to provide specific details on the COVID -- on the impact of COVID-19 for each one of our trials, we can say that we have seen an impact across all of our trials to varying degrees. Our most effective trial is pamrevlumab's ZEPHYRUS IPF trial where we decided to pause near-term enrollment for the safety of patients and are currently focused on providing continual care for the patients who had already been enrolled. The rest of our trials continue enrollment, albeit, at a slower rate.

In 2020, we are committed to accelerating and expanding the development of pamrevlumab. To that end, we have developed a comprehensive plan, which includes clinical site activations, geographic expansion and protocol amendment, such that, once things return to a new normal, we can be in the best position to accelerate enrollment.

Our locally advanced unresectable pancreatic cancer study continues to enroll. We continue preparations for ZEPHYRUS 2, our second IPF Phase III study, and our Phase III program in Duchenne muscular dystrophy is slated to begin in the second half of the year.

In summary, despite COVID-19, we continue to be focused on getting roxadustat approved in the U.S., advancing pamrevlumab development; and finally, leveraging our expertise in both hypoxia-inducible factor, and connective tissue growth factor biology to expand our pipeline of novel drug candidates.

Now I will turn it over to Peony, who will provide you with a more in-depth discussion of roxadustat.

K. Peony Yu

Chief Medical Officer

Thank you, Enrique, and good afternoon, everyone. Our 2020 start has been busy. And today, I would like to review some of the roxadustat highlights thus far this year.

As Enrique mentioned earlier, we continue to expect an FDA decision on our roxadustat NDA by the PDUFA date of December 20, 2020. We have no indication the FDA will hold an Advisory Committee Meeting, but we continue to prepare diligently in case, one is scheduled.

To ensure success in the U.S., we and our partner, AstraZeneca continue commercialization preparations. We plan to submit our Phase III individual study and pool efficacy and safety manuscripts for publication over the coming months.

In Europe, the Marketing Authorization Application filing for roxadustat for treatment of anemia in both dialysis- and non-dialysis-dependent CKD patients is expected in the second quarter of 2020.

In Japan, our partner, Astellas, continues the commercial launch of Evrenzo, the Japan brand name for roxadustat for treatment of anemia in dialysis-dependent patients. Astellas' supplemental NDA for anemia in non-dialysis patients is currently under review by PMDA.

We recently presented new analyses from our Phase III roxadustat trials at the annual National Kidney Foundation Spring Clinical Meeting.

And the conclusions can be summarized as following: in our non-dialysis patients, roxadustat achieved comparable hemoglobin correction with similar doses regardless of iron status at baseline. Roxadustat treatment resulted in a statistically significant reduction in red blood cell transfusion risk of 74%. 40% of the patients in this non-dialysis patient pool were not iron replete or did not have sufficient iron stores to even qualify for ESA treatment.

Furthermore, roxadustat reduced the risk of red blood cell transfusion and IV iron rescue compared to placebo in non-dialysis CKD patients, regardless of iron status at baseline.

Finally, roxadustat significantly reduced the risk of red blood cell transfusion in dialysis patients versus epoetin alfa.

Let me point out roxadustat's reduction of transfusion risk goes hand-in-hand with the superior hemoglobin efficacy achieved in our primary endpoint analysis compared to EPO. Roxadustat's superior hemoglobin change and transfusion reduction are accompanied by favorable cardiovascular safety results, particularly.

In the 1,530 patient incident dialysis pool, roxadustat had a 30% lower risk of MACE and 34% lower risk of MACE+ than epoetin alfa. This is highly relevant as 86% of U.S. dialysis patients have now received ESA therapy in the 12 months prior to the initiation of dialysis.

Collectively, these results give us confidence that roxadustat may have a differentiated product profile for dialysis-dependent patients. Beyond CKD, our vision is for roxadustat to become the standard of care for anemia broadly. We continue development of roxadustat for the treatment of anemia associated with myelodysplastic syndrome, or MDS, and chemotherapy-induced anemia, or CIA.

We also continue to evaluate roxadustat for the treatment of anemia associated with additional diseases. Starting with our Phase III global study evaluating roxadustat for the treatment of anemia in MDS, we presented positive results from open-label portion of this study at American Society of Hematology 2019 and are now conducting the randomized double-blind placebo-controlled portion of the study. As a reminder, this second portion of the study will enroll approximately 160 transfusion-dependent MDS patients in a 3:2 randomization, and the primary efficacy measure is percent of patients who achieved transfusion independence.

Staying in the hematology/oncology space, we also have an ongoing Phase II open-label study in CIA, which continues to be an unmet medical need. We will continue to monitor, assess and manage the impact of COVID-19 with patient safety as our top priority. We thank all our investigators for their commitment and partnership in developing new treatment option for patients.

Finally, in collaboration with our partner, AstraZeneca, roxadustat Marketing Authorization Application for CKD anemia have been submitted in a number of countries, including Canada, Australia, Mexico, Brazil, Taiwan and South Korea.

I would now like to turn the call over to Chris Chung who will discuss the recent developments for roxadustat in China.

Christine L. Chung

Senior Vice President of China Operations

Thank you, Peony. I'm excited to share details of the positive progress made during the first quarter on the roxadustat launch in China. As many of you know, roxadustat was included in the 2019 National Reimbursement Drug List last November. It became effective January 1 of this year, and the government is ensuring that rollout is completed on an accelerated basis.

Hospital visitings have been a key focus of our large efforts and the top priority of the AstraZeneca-dedicated roxadustat sales team. We are pleased with our progress to date. Roxadustat is now listed and available at many hospitals within our target universe. We are particularly pleased with the penetration as top-tier Class 3 institutions, which are the larger accounts and also where key opinion leaders and early adopters practice. We believe the hospitals where we are listed to date represent greater than 30% of the potential CKD anemia market opportunity in China.

Roxadustat net sales were just under \$5 million for the quarter. Q1 represents the first quarter after the inclusion of roxadustat in NRDL, and obviously, sales were affected by the COVID-19 pandemic.

From late January through the end of February, China was essentially locked down, and sales visits were completely stopped. During that time, physicians and hospitals were largely focused on treating COVID-19 patients. The number of non-dialysis outpatient visits were highly impacted and dialysis visits were also affected but to a lesser degree.

Looking forward to Q2, we expect our operations in China to return to a new normal, where social-distancing rules will continue to apply. Sales representatives are now able to conduct sales visits, and hospital visiting committee meetings are being scheduled. Many forms of scientific engagement have moved to digital, where disease education, case discussions and roxadustat experience of sharing are now being conducted primarily online, in a virtual manner. We have seen roxadustat utilization across different patient populations, including hemodialysis, peritoneal dialysis and non-dialysis and in both ESA naive and ESA-treated patients.

We continue to be encouraged by the unique value proposition of roxadustat in the treatment of anemia and CKD, in particular, within the treatment setting in China, given the reduced need for intravenous iron to achieve target hemoglobin levels, even in the presence of inflammation as well as the oral route of administration.

We look forward to keeping you updated as we advance our work towards the long-term goal of making roxadustat the standard of care in treating CKD anemia patients in China.

I will now turn the call over to Elias who will provide an update on the pamrevlumab program. Elias?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Thank you, Chris, and good afternoon. Today, I would like to provide an update on our pamrevlumab program given the COVID-19 development over the recent months.

As you all know, we are developing pamrevlumab in 3 separate orphan diseases. At the time of our last earnings call, we were enrolling ZEPHYRUS, a randomized double-blind, placebo-controlled Phase III study evaluating pamrevlumab in IPF and announced plans to initiate a second similar Phase III trial in IPF named ZEPHYRUS 2.

Given the recent COVID-19 pandemic, in order to ensure patient safety in this vulnerable population with compromised lung function, we have decided at this time to temporarily pause enrollment of ZEPHYRUS Phase III clinical study.

The safety of our patients is our top priority, as we continue to assess this dynamic situation and we continue to work with investigators to provide care and clinical trial continuity for patients who are already enrolled in this trial. Prior to posing enrollment, we were focused on accelerating enrollment of our ongoing ZEPHYRUS Phase III study in preparing to initiate the ZEPHYRUS 2 trial. To the extent possible, we continue these preparations, such as when we are able to restart enrollment, we will hit the ground running.

Moving on to our locally advanced unresectable pancreatic cancer, or LAPC, program. LAPIS is our ongoing randomized double-blind, placebo-controlled Phase III trial in patients with LAPC. As you know, these patients have a great prognosis, and we are working with our investigators and clinical trial site staff to implement changes, which mitigate the risk to patient and comply with regulatory and government quidance.

We continue to prepare to initiate a Phase III trial, LELANTOS, evaluating pamrevlumab as a treatment for Duchenne muscular dystrophy, or DMD, in the second half of 2020. There is a significant interest for DMD health from the DMD health care providers and patient communities. This global trial will be a randomized double-blind, placebo-controlled Phase III trial of pamrevlumab in patients with non-ambulatory DMD. It will enroll approximately 90 patients randomized 1-to-1 to placebo and have a treatment period of 52 weeks.

Now I will turn the call over to our CFO, Pat Cotroneo, for the financial update. Pat?

Pat Cotroneo

Senior VP of Finance & CFO

Thank you, Elias. As announced today, total revenue for the first quarter of 2020 was \$24.4 million as compared to \$23.9 million for the first quarter of 2019. The current quarter revenue consists of \$19.4 million in development revenue plus net product revenues of \$5 million for roxadustat sales in China. For the same period, operating costs and expenses were \$105.5 million and net loss was \$78.3 million or \$0.89 per basic and diluted share as compared to operating costs and expenses of \$72.7 million and a net loss of \$45.4 million or \$0.53 per basic and diluted share for the first quarter this year.

Included in operating costs and expenses for the quarter ended March 31, 2020, was an aggregate noncash portion totaling \$22.1 million, of which \$16.9 million was a result of stock-based compensation expense as compared to an aggregate noncash portion of \$20.4 million, of which \$16.4 million was a result of stock-based compensation expense for the same period in the prior year. At March 31, FibroGen had \$598.4 million in cash, cash equivalents, restricted time deposits, investments and receivables.

As previously stated, in accordance with the U.S. GAAP, we recognized in our Q2 2019 financial results a total of \$180 million of milestone payments, when achievement became probable. The amount was comprised of \$50 million for anticipated milestone from AstraZeneca related to the filing of the U.S.

NDA, which was received on April 1, 2020, and \$130 million in anticipated milestones from Astellas in connection with the EU MAA filings, which we expect to occur in the second quarter this year.

Based on these milestone payments and our latest forecast data, we continue to estimate our 2020 ending cash balance of cash, cash equivalents, restricted time deposits, investments and receivables to be in the range of \$720 million to \$730 million, assuming U.S. NDA approval in Q4 2020.

Looking ahead, we have a total of \$375 million in anticipated milestones expected over the next 15 months for the U.S. and Europe, which includes the aforementioned \$130 million of milestones for MAA submissions, plus \$245 million of milestones on approvals and first commercial sale. At this point in time, we have no changes in expectations in any of the anticipated milestones over the next 15 months. Thank you.

And I would now like to turn the call back over to Enrique.

Enrique A. Conterno

CEO & Director

Thank you, Pat. In closing, FibroGen is well positioned to navigate these uncertain times. We and our partners are committed to making roxadustat available to as many patients across the globe as quickly as possible. We have ample supply of roxadustat drug product to meet demand for the year and ample supply of pamrevlumab for our planned clinical trials.

As roxadustat sales ramp up, our financial position is strong with approximately \$600 million in cash at the end of the first quarter. We have a total of \$375 million in anticipated milestones expected over the next 15 months in the U.S. and Europe, which includes \$130 million of milestones for the MAA filing, plus \$245 million of milestones on approvals and first commercial sale.

In addition, we received full-partner reimbursements for development and commercialization of roxadustat in all geographies, except China, where we share these expenses 50-50 with AstraZeneca. Based on our current forecast, we are reiterating our estimated 2020 ending cash to be in the range of \$720 million to \$730 million and continue to believe we are well financed for years to come.

Now I would like to turn the call back to the operator for questions. Operator?

Question and Answer

Operator

[Operator Instructions] Our first question comes from Michael Yee with Jefferies.

Michael Jonathan Yee

Jefferies LLC, Research Division

Enrique, Peony, guys, two questions from me, if you can hear me, okay?

Enrique A. Conterno

CEO & Director

Yes.

Michael Jonathan Yee

Jefferies LLC, Research Division

There was recently some competitor data that came out this week. Maybe you can just talk about how to put that into context. Importantly, in the dialysis segment, they only had 10% of the population and incident, where you had, I think, upwards of 40%, yet you guys have the same hazard ratio of 0.96. So maybe talk to that data set? And what that would mean, both in incident dialysis and stable dialysis, when you try and compare that data? And then my second question is on China. Chris, I thought you had some good comments there. Maybe talk about how you expect Q2, 3, 4 to ramp as people are modeling sales.

Enrique A. Conterno

CEO & Director

Very good. Thank you very much, Michael, for the questions. I'm going to turn over the question on the recent competitor data to Peony, but let me just make a comment on that. Clearly, this data validates HIF-PHIs, I think, in an important way. But I'm excited for us to be able to also share why are we so excited about roxadustat in terms of the differentiation.

And we will then go to Chris for your questions in China in terms of sales ramp-up. Peony?

K. Peony Yu

Chief Medical Officer

Thank you, Enrique, and thank you, Mike, for asking the guestion. Recent data reaffirms the safety of the HIF class, as Enrique said. In addition, we are reassured that the roxadustat product profile is compelling. This is a great opportunity to remind us about the differentiating aspects of roxadustat.

From an efficacy standpoint, roxadustat is numerically and statistically superior in hemoglobin efficacy endpoint, which then, in turn, translates into clinical benefit of reduction of transfusion in dialysis patients. Our primary efficacy endpoint of change from baseline to weeks 28 to 52 was superior to an active comparator after we met noninferiority comparison. And the P-value is less than 0.001.

Now what is very -- we also have statistically significant reduction in transfusion risk. Importantly, we have demonstrated cardiovascular safety in the overall dialysis population and in MACE. And furthermore, we demonstrated a reduction in MACE+ risk. In our 1,530-incident dialysis patient pool, where the comparison between roxadustat with epoetin alpha started within the first 4 months of dialysis initiation, roxadustat had a 30% lower risk of MACE and 34% lower risk of MACE+ than epoetin alfa, with a trend towards lower or cause mortality, relative to epoetin alfa. Now this is a highly-relevant population. The difference between the incident dialysis and the stable dialysis is that, incident dialysis describes the point of entry, timing of the entry into the study. Patients -- this includes patients who have started dialysis within 4 months of study enrollment and continue receiving treatment well into stable period as the average treatment is around 2 years.

And to address the question of -- that you have brought up about stable dialysis, the other subgroup of the all dialysis patients are patients who entered the study at the time that they have been on dialysis for more than 4 months and continued treatment. When we look at the converted patients or the stable dialysis patients and evaluate and looking at safety -- cardiovascular safety, it does not change any of the conclusions that we have on the -- about roxadustat being safe and efficacious.

And so in conclusion, roxadustat, excellent cardiovascular safety profile, coupled with the statistically significant and clinically meaningful, higher hemoglobin efficacy results and lower transfusion rate relative to epoetin alfa, together makes roxadustat potentially a better treatment option for dialysis-dependent patients. We like the hand that we have and expect the product label to reflect the results of clinical trials on our compound.

Michael Jonathan Yee

Jefferies LLC, Research Division

I appreciate the question because, yes -- because of the stable population and doing the math around that versus them. So incident is important, and I appreciate the response. And maybe Chris, on China?

Enrique A. Conterno

CEO & Director

Chris?

Christine L. Chung

Senior Vice President of China Operations

Yes. Mike, so we continue to be optimistic about second, third and fourth quarter. The way to look at the numbers might be, you saw the Q4 numbers and you saw the Q1 numbers. So what does the Q1 numbers tell you? So there is seasonality in terms of when the things typically come in, in China. So as you know, without listings, you cannot prescribe. So these things are key, but also, there's tremendous momentum coming out of NRDL to list because it makes the drug affordable and it makes hospitals wants a list. So we are very happy with the Q1 numbers. It reflects momentum coming out of NRDL. It reflects a bit of a slowdown because of COVID. We're now coming out of COVID into new normal. It's a little bit touch-andgo, so it's hard to predict based on it, but we continue to be very optimistic in what the rest of the year looks like.

Operator

And our next question comes from Geoffrey Porges with SVB Leerink.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

In NDT versus DD, I'm curious, Chris, first of all, in China, what's your assessment of how this will play out over the long term? Hypothetically, do you think that they're roughly equal? Or do you think that one is going to ultimately be significantly larger than the other?

And then, Enrique, I know you're not responsible for commercialization, but I'd love to hear your color on what you think the situation will be in the U.S. again? Do you think that the opportunity will be larger in dialysis, given your incident dialysis data? Or do you think that the greater opportunity will be getting the non-dialysis claim?

Enrique A. Conterno

CEO & Director

Very good, Geoff. Let me try to address both of your questions. Looking at the relative size of both dialysis and non-dependent-dialysis, clearly, the number of patients that have anemia, and that are on dialysis is significant, but the opportunity to help patients in non-dependent-dialysis is, of course, much, much larger. I view both opportunities as important opportunities. But over time, I view the opportunity in non-

dialysis-dependent patients to be much larger than the opportunity in the dialysis. Of course, we will need to do our job to ensure the patients are accessing treatment for anemia, patients that have CKD.

When it comes to the U.S., I know you give in a minute this way, but I am completely engaged when it comes to ensuring that we can have a successful commercialization of roxadustat. And I had the opportunity to engage, of course, with AstraZeneca. The situation there follows, I think, similar comments in China being the NDD opportunity over time, has a potential to be significantly larger as we develop that market and we ensure that patients are treated. Keep in mind that when we look at patients coming in to dialysis today and we look at the prior 12 months, only about 14% of them are treated for anemia in those prior 12 months. So a great opportunity, I think, to ensure that many, many patients get appropriately treated and clearly, a huge opportunity for market expansion there.

Operator

Our next question comes from Jason Gerberry with Bank of America.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Yes. Just curious, if you can comment on your 2020 roxa publication strategy. I imagine your competitor will be looking to make a splash in ASN later this year. And so I know that there's some data points regarding the roxa program, for instance, the data on the MACE subcomponents for the DD study. Just curious, if we could get any more incremental data published out of you guys later this year? And if you can comment at all on that front. And then maybe just a follow-up for Chris. Help us think about the \$5 million number for China this quarter. Is that a pure demand-driven number? I assume, inclusive of the COVID headwind. You mentioned 30% of hospitals have access to roxa, but I think in prior conversations, you talked about the NDD market requiring more market building. So should we think about that access as being more around the DD opportunity, at least at the onset?

Enrique A. Conterno

CEO & Director

Yes. Thank you, Jason, for the question. I'm going to ask Peony to comment on our publication strategy. We are excited about the publications that we are -- publication planning, what we're trying to do this year. And then I'm going to ask Chris to give us some more color on China. Peony?

K. Peony Yu

Chief Medical Officer

Yes. I am very excited about our upcoming publication plans. We could -- I can say that we are data-rich, and we're working very closely with our 2 partners, Astellas and AstraZeneca, to -- we are committed to submit our Phase III individual studies as well as pool efficacy and safety manuscripts for publications over the coming months. We also plan to submit a number of abstracts to ASN, which will be held in October of this year. Stay tuned.

Enrique A. Conterno

CEO & Director

I'm -- yes, Chris, if you could please answer the question on China, provide little more color.

Christine L. Chung

Senior Vice President of China Operations

Absolutely. So Jason, you asked if the \$5 million is a pure demand number. So the answer is no. The \$5 million represents ex factory revenues from FibroGen Beijing into the channel. In particular, it represents net revenues, which is orders minus VAT, which is 13%, net or distributor's discounts, incentives, commissions. So it's really a pure net numbers into the channel. The difference between the channel inventory, the demand number is the gap. So this is not a demand number. It's a net ex factory number.

The second question, Jason, I believe you asked is whether this represents more DD versus NDD. So what we have seen so far is very consistent with what Enrique said just now. In the long term, the NDD market has more patients, and we can have a significant impact in that patient population because they're currently either not treated or undertreated. But that is a market we need to build. For DD, it's a substitution market. It's a very well-established standard of care and treatment pattern, where either people are converting from standard of care to HIF-PHIs or incident patients are starting with HIF-PHI. We have seen adoption across all the patient types, which is hemodialysis, peritoneal dialysis and very encouragingly, non-dialysis. So the number you're seeing in terms of revenues is shift in from our factory into the channel based on demand from HD, PD and NDD.

Enrique A. Conterno

CEO & Director

If I -- yes, if I could just complement a bit. As you know, Jason, I had responsibility for China as well, when I was at Lilly. To be able to have basically a 30 -- access to 30% of the overall market opportunity post-NRDL listing, I think, is very significant. So we -- that's a great progress. We used to take companies post-NRDL listing basically years to be able to have meaningful market access opportunity in China. I think that's extremely encouraging. I do want to make sure, there wasn't anything, while the \$5 million are just the ex FibroGen sale, net sales, there's nothing unusual when it comes to stocking. The stocking was very normal for the quarter. And I would say, as we look at Q2, Q3 and Q4, we do expect a meaningful rampup.

Operator

And our next question comes from Adam Walsh with Stifel.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

This is Edwin on for Adam. First one, on COVID-19. We know there are published studies showing that COVID-19 patients, even those who have recovered are suffering from long damage, including fibrosis. So do you have any plans to explore pamrevlumab or other pipeline assets in this COVID-19 patient? And I have a follow-up, if I may.

Enrique A. Conterno

CEO & Director

Yes. Thank you for your question, Adam. I'm going to ask Elias to comment, but just we are planning to study pamrevlumab in hospitalized patients with COVID-19. And we see 2 potential applications in the acute setting, to improve oxygenation and also in the post-acute setting, to ameliorate lung fibrosis.

I'm going to ask now Elias to make a few more comments or reasons to why we are excited about this additional opportunity to be able to help patients with COVID-19. Elias?

Elias Kouchakji

Senior Vice President of Clinical Development, Drug Safety & Pharmacovigilance

Thank you for your call. So as Enrique is saying, we are looking at these studies currently, and we're discussing these studies with regulators, such as the FDA and other European regulators. We are moving forward with planning for these studies. And the difference is, as we know, there is 2 stages of the COVID-19: the acute phase, the first 15 days; and the residual phase. In the acute phase is -- there is a big lack of oxygenation, which is obviously, is important part that is leading to a lot of difficulties in treating these patients. Pamrevlumab is -- can have some effect. We have some data that to show, that is -- we can affect the leakage at the level of the vessels in [introduced] edema and might facilitate oxygenation. And the long-term said that this patient is showing interstitial lung fibrosis and lung disease, specifically after the Acute Respiratory Distress Syndrome. In IPF, we have shown our good effects on fibrosis, and we believe that this potentially that CTGF is similarly is affecting fibrosis, which we know it is from our radiation-induced lung fibrosis that we can slow down or stop that progression of the fibrosis. And we are planning forward to discuss these studies soon and planning to move forward with them.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

Great, great. My next one. Earlier this week, a competitor discloses upper bounce of noninferiority margin of 1.25, which is agreed by the FDA. Should we assume that it is the -- you -- hold you to the same standard or review and approval?

Enrique A. Conterno

CEO & Director

Yes. Thank you. I will try to answer this pretty quickly. I think we have as stated this before. We feel that the overall cardiovascular data that we basically have on both DD and NDD is quite compelling. And we feel that roxadustat presents an important -- has an important benefit risk ratio. As we stated before, questions about noninferiority will be a part of a review decision for roxadustat, but we feel very confident in terms of what we have been able to show and the benefit risk profile that the product has.

Operator

And our next question comes from Yaron Werber with Cowen.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And congrats on China. I mean it looks like it's off to a really terrific start. I had a quick question relating to -- maybe just your thoughts, and I don't know if you can comment a little bit ahead into the U.S. launch, early next year, in the dialysis setting and specifically, with the benefit of TDAPA. With TDAPA drugs like roxa should, once included, have a financial incentive to get used. Earlier, I think it was last week, Amgen noted that Parsabiv has seen a decent uptick in small and sort of medium-sized dialysis clinics, but much -- face much bigger headwind sort of really getting into DaVita and Fresenius. So thoughts about, sort of how would you tackle that to make roxa sort of more attractive for them. And then I have a quick follow-up as well.

Enrique A. Conterno

CEO & Director

Yes. Thank you. I think -- thank you for your question. Clearly, TDAPA offers, I think, an incentive to make sure that innovative products are included as part of the treatment protocol for dialysis centers. And I think it's designed for a product such as roxadustat.

Just to maybe speak a little bit about the process. Once we receive approval, we will have to submit for -to be reimbursed under this system, this TDAPA system. We expect that within 3 months, we will be able
to get that designation. And clearly, as we think about that, just like we will be preparing for any launches,
clearly, in this particular case, the large dialysis organizations are key in terms of their adoption, and you
can be reassured that we are, and AstraZeneca, is working closely with them to ensure that we can have
the very best adoption possible and ensure that innovation is included in the treatment of patients in the
dialysis centers, and that is included fast. So I can't speak for other companies, but I feel good about the
plans and how we're solidifying those plans now.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Okay. And just another question. At sometimes, Peony, I think maybe you touched upon this, do you have plans to release the data for the prevalent dialysis on its own? I mean you've done really a terrific job showing us the incident dialysis data and overall dialysis. And just curious about the prevalent dialysis as that accounted for about 80% of patients in the market.

Enrique A. Conterno

CEO & Director

Yes. I'm going to ask Peony to address the question. I assume it is talking about the stable dialysis. Peony, any -- what are our plans when it comes to releasing that particular data?

K. Peony Yu

Chief Medical Officer

Yes. As I mentioned, our incident dialysis data also contains prevalent dialysis data in that. Incident was the first 4 months, that's the entry into the study, and patients continue receiving treatment. And so they are the prevalent patients. And I've mentioned earlier that we have looked at the patients who -- the stable dialysis or the prevalent dialysis patients who have been on dialysis for 4 -- more than 4 months at the time that they enter our Phase III study. And we are very comfortable with the efficacy and the safety data in that subgroup. And that's -- the results does not change our conclusion or confidence about our product. And there, it is very likely that we will -- we may share this data, and I wanted to remind ourselves that, that was not necessarily a -- that analysis was not a prespecified analysis. And so we are still comfortable with it. And the most important, to keep in mind is that the overall data, overall dialysis, which was the prespecified analysis and that we have already disclosed that and reiterate that the 86% of the patients who start dialysis have not had received any ESA treatment for the anemia. And therefore, incident dialysis where we take those patients within the first 4 months into the study, and we consider that data to be highly relevant. And we believe that we may have the largest incident dialysis patient pool in CKD anemia programs.

I'm sorry. Enrique, did you want to add something?

Enrique A. Conterno

CEO & Director

Yes. Thank you, Peony. I -- the only thing that I wanted to add Yaron, was you talked about the incident dialysis being 20% of the market. I think it's -- that's correct for the first year, right? You're thinking of -- but unfortunately, the mortality of patients in dialysis is very high. So having a product that is differentiated in incident dialysis is given that it's a natural point for a treatment decision, when it comes to anemia starting dialysis. We found it's particularly important in order to have preference for that treatment. And we believe that roxadustat is uniquely -- is going to be uniquely positioned there. Thank you.

Operator

And our next question comes from Paul Choi with Goldman Sachs.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Maybe my first question is for Peony and with regards to the double-blind portion of the Phase III MDS trial. Can you maybe just comment on -- are you seeing -- thinking about any potential impacts to time lines, just given that the patients have to be conditioned for their MDS treatment before potentially receiving roxa? And then, I had a follow-up on Europe.

Enrique A. Conterno

CEO & Director

Peony, go ahead.

K. Peony Yu

Chief Medical Officer

Yes. I wanted to clarify that unlike -- look, a [matter of] product trial, in terms of trial design, our MDS trial includes patients who are treatment-naive and those who have failed ESA. And then, we are also includes patients who are ring sideroblast positive and ring sideroblast negative. The trial is a global study and include study sites and patients in the U.S. and in Europe. I hope that answers.

And then, we are now at the double-blind, placebo-controlled portion of the study. And as you alluded to, I just wanted also remind ourselves that we have a share of very encouraging positive data of the open-label segment of this study at the American Society of Hematology in 2019. I hope that answered the question.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

I guess maybe to put it in a different way, Peony, just given the situation with COVID and the risk to MDS patients, who have to go through chemotherapy or conditioning, do you see any changes to the time line for your Phase III?

K. Peony Yu

Chief Medical Officer

Oh, okay. Now I wanted -- actually, there is a little impact on our trial -- on a Phase III trial for the following reasons, because now the patients we enroll are already transfusion-dependent. So they are -- they do need to be monitored and treated by their physician, or in other words, they're tethered to the health care system. And participation in our trial, where we provide an oral medication to reduce the risk of transfusion, it's view, if you can think about this -- think about it this way, that it could be favorable, if patients could have less -- will require less transfusion. That can translate into less exposure risk. Does that make sense?

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Yes. That's helpful. And then regarding Europe, as you're approaching the MAA here in the coming -- end of this quarter, and as you look maybe on the forward here and think about commercialization, just with regard to the different European views on using roxa in the 2 populations, can you maybe comment on how you expect adoption might go there between yourself or what your partner might see as you think about the early launch curve there?

Enrique A. Conterno

CEO & Director

Yes. Clearly, as we have stated, we are expecting filing in Europe this second quarter. And clearly, as you know, when it comes to Europe, different markets behave differently. This is a good question for Astellas, but we need to keep in mind that in some markets, you can make the product -- you can launch the product right away, like in Germany and so forth. In some other markets, you need to go through -- be able to get some reimbursement. So there's going to be a market-by-market decision, and we look forward to helping as much as we can, Astellas as they're really the drivers when it comes to commercialization, of course, in Europe.

Operator

And our next guestion comes from Difei Yang with Mizuho.

Alexandre N. Bouilloux

Mizuho Securities USA LLC, Research Division

This is Alex on for Difei. I was wondering if you could comment a little bit on the NDD setting in the U.S. Specifically, I was interested in -- if you could talk about what is the standard of care there. How are ESAs used today? And what do you think are the benefits of having a placebo comparator in that setting? And then along with that, I was wondering whether or not you would expect the black box warning on approval?

Enrique A. Conterno

CEO & Director

Very good. I'm going to try to pass this to Peony. I'll try to answer the last part of your question. Clearly, I think what we said is that the data, the data that we have, we do not believe wants a black box, but this is a decision for the regulators. I'm going to ask Peony to comment on NDD and the standard of care. Unfortunately, many patients are not treated for anemia that do have anemia. And so there's an opportunity for -- to improve the treatment rate. But Peony, you can talk about the standard of care and maybe provide some color in the United States.

Peony?

K. Peony Yu

Chief Medical Officer

Sorry, I just -- thanks for reminding me to be unmuted. So thank you for the question. We do believe that non-dialysis-dependent patients, anemia is largely an unmet medical need, and this offers a great opportunity for roxadustat to improve care in this population. What I mean by that is that because of cardiovascular safety concern of ESA, their treatment of non-dialysis patients with ESA is limited to keeping hemoglobin less than 10. And in the literature, there's extensive evidence that keeping patients hemoglobin less than 10 is associated with higher transfusion risk. And so there is well-known that, since the label change in ESA in 2011 that the transfusion rate has gone up in the non-dialysis patients, along with the reduction in the treatment rate of non-dialysis patients. And this is reflected by the USRDS data of only about 13.5% of the patients entering dialysis have been exposed to ESA in the 12-month prior.

What does this translate for roxadustat? This is the main reason that we have chosen placebo as the comparator, since no care is the standard of care in the U.S. And in our Phase III program, we have demonstrated a significant increase in hemoglobin level compared to placebo and importantly, significantly reduced transfusion to only about 1/3 of the placebo. And now in -- and our treatment resulted in hemoglobin at around 11, and this was our treatment goal.

And so I also wanted to point out that placebo comparator offers as a comparator is a high bar for comparison for cardiovascular safety because, if one were to choose ESA, that -- as an agent, that already has a box warning for cardiovascular safety. But placebo is the gold standard. With -- in comparison to placebo, we have demonstrated that cardiovascular safety in the MACE endpoint and MACE+ endpoint.

Finally, finally, our talk does not -- in our program, 40% of our patients were not iron repleted, which is a requirement for ESA. So not only are we able to treat the patients to a more therapeutic level of hemoglobin and reduce transfusion, we are going to be able to expand treatment to more patients, even when they're -- they don't have as much iron around. Thank you.

Enrique A. Conterno

CEO & Director

Very good. Thank you, Peony. And I know that we are -- we have already extended our time. So I want to thank everyone for joining our call and for all of your support of FibroGen. Thank you. Thank you very much.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for participating, and you may now disconnect. Everyone, have a great day.

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EXHIBIT Y

S&P Global
Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Thursday, May 14, 2020 4:00 PM GMT

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Call Participants

EXECUTIVES

Enrique A. Conterno CEO & Director

ANALYSTS

Jason Matthew Gerberry BofA Merrill Lynch, Research Division

Presentation

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Good day, everybody. My name is Jason Gerberry. I cover smid-cap biotech and specialty pharmaceutical for Bank of America. I'm pleased to be introducing our next company presenter, FibroGen and new CEO, Enrique Conterno. FibroGen is -- most would know the company for its development of roxadustat for anemia associated with dialysis or renal disease, but the company also has an emerging early-to-midstage pipeline with pamrevlumab for fibrotic disorders.

So Enrique, first off, thanks for joining us at the conference on a virtual basis.

Enrique A. Conterno

CEO & Director

No, thank you, Jason. It's a pleasure for me to be here and talk about the progress we're making at FibroGen.

Question and Answer

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Great. I mean, look, you're no longer new to the role, but I imagine that the opportunity with roxadustat was an important factor as to why you joined the company. As we look at the marketplace for anemia disorders associated with renal disease and chemo-induced anemia, we once upon a time saw almost a \$10 billion market. That's obviously compressed as a result of some label restrictions around the current standard of care. But I'm curious, your views on the HIF class, which is where roxadustat is a drug within. Your thoughts, from a commercial standpoint, can the category get back to those historical peak levels, either on a combined basis or even if the market more gradually or rapidly migrates to HIFs? So maybe we can start there.

Enrique A. Conterno

CEO & Director

Sure. So -- and I think you got it right. I think I -- yes, I joined FibroGen in early January, and part of the reason I joined is, I saw the promise with this transformational medicine for anemia, generally, of course, first, in -- when it comes to CKD. And my answer would be, yes, not only to get to the previous levels when we think about the overall anemia treatment but beyond that. And I think we have to keep in mind that the use was there, the category was larger at that point in time. And the reason we basically saw some of the declines in the category were related to some of the restrictions on the labels for ESAs. Now clearly, all of this needs to come in the context of data. And in particular, I'm excited to talk a little bit more about roxadustat and how I view that when it comes to the data that we have in CKD. And maybe that will be the next section. But clearly, we're also studying roxadustat in chemo-induced anemia, in MDS, and we do have a portfolio of other opportunities that we're looking at for us to truly, not just pursue anemia in CKD, like we are today, where we have the submission accepted in the U.S., expected to submit in Europe in Q2. Commercially, having success in both China and Japan. And of course, that's key, but eventually, we want to make sure that we're treating all sorts of anemia with the promise that roxadustat has.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Got it. Great. And as we think about where the market once was, where it is now, some of the major haircuts, and correct me if I'm wrong, were the CKD stage 3/5 treatment rates have come down quite a bit. The treat to target, the quantity of drug for a class that was priced on a quantity basis in dialysis has gone down. And then the lack of the chemo-induced anemia market has taken a massive hit because of the safety perceptions or implications, however you want to frame it. So from your perspective, are one of those levers really what you see as more near term and sort of the clear opportunity in front. I would imagine it would be the CKD 3/5 treatment rates might be sort of the key low-hanging fruit here, whereas the chemo-induced anemia opportunity probably is a longer-term type of driver.

Enrique A. Conterno

CEO & Director

I think, yes. And I think we do just because of the sequence of how we pursue these indications. Clearly, we are very near the action date by the FDA that's expected, December 20 of this year. And basically what we see and I think you said it well, when it comes to dependent dialysis patients, yes, those patients continue to be treated for anemia, 95% of them. That's -- so the use there on the treatment side, I think, continues. But when it comes to nondependent dialysis, I think we've seen a huge drop off in terms of treatment rates. Today, in fact, what we basically see is for -- when we look at the 12 months prior to going onto dialysis, we see about 13% to 14% use of ESAs in that patient cohort. That number used to be as high as 30%. So clearly, there's a huge opportunity to scale that market up. That needs to be driven by the data. And we think that we have the data to try to support a massive shift in terms of ensuring that anemia is treated in a safe way in patients, both that are dialysis-dependent or nondialysis-dependent.

So that is a more near-term opportunity just because that indication is coming first. But we are pursuing chemo-induced anemia, and we see a pretty large opportunity there as well.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Great. And before we jump into some of the details, how do you see it all fit in? Do you see -- you've got potentially biosimilar ESAs, branded ESAs, potentially multiple HIF in-class competitors? Do you see this market as a dominant treatment option? Do you see the market being more fragmented based on what we know today?

Enrique A. Conterno

CEO & Director

Yes. I -- clearly, I think like any other market I think it's going to depend on the data that the new entrant -- that the new products basically bring and the differentiation that they bring into -- and becoming new standards of care. And I think in this particular case, I think it's pretty significant. I think it's -the differentiation of roxadustat, I think is quite meaningful when -- and I'd like to focus on maybe 3 points. And the differentiation that I think about is not just relative to current treatment, but maybe other potential future treatments. Because keep in mind that FibroGen have -- or had and have the largest library of HIF-PHIs. And there are a number of compounds that the company looked at. And the reason roxa was picked is because we felt it basically provided the best benefit-risk profile for treating anemia. So the -- as I think about this particular class, which, by the way, was further validated by one of our competitors for using data. But in particular, as I think about the differentiation of roxa, number one, I think you have to start with efficacy. Keep in mind that not only do we meet our primary efficacy end points, we were basically statistically superior to EPO on our trials in DD. So that's important. Of course, we also show efficacy. It was relative to placebo in NDD. And quite -- when we look at -- one of the benefits of having achieved efficacy when it comes to hemoglobin is that it translates into lower transfusion rates. We actually had lower transfusions with roxa than with EPO, and of course, much lower relative to placebo in the NDD segment. So that benefit to me, I think, is pretty significant. Clearly, in the -- when we look at the totality of the data, I find our overall cardiovascular data pretty compelling. And in particular, I think we need to highlight the incident dialysis data, whereby we basically show a reduction in risk of MACE events at a time that is critical. And this is -- incident dialysis, basically, covers those patients within the first 4 months of starting dialysis. That is the time when a treatment decision is made when it comes to anemia. So I feel like we are perfectly accurate to wish -- with a huge benefit in that cohort of patients, to be able to have a significant position longer term in that segment. So that I find also quite meaningful. And clearly, the data is highly -- it was -- compared to EPO, it's highly differentiated based on what we can see. And finally, I think something that maybe people don't emphasize as much, but I think we need to keep in mind when we look at the overall NDD segment and we look at the broad spectrum of patients that we were able to enroll, including iron-replete and non-iron-replete as well. So those -- we had a broad spectrum of patients that were -- basically were enrolled in the trial. And I think that's going to be an element of differentiation longer term as well for the product. So I like the chances that given the outcome that are so meaningful with this particular product.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Okay. Now the U.S. market, it's an important market. If you look at consensus, I think that The Street does view the U.S. as a particularly important market. So mindful that this is a process that's being driven, I presume, by your partner, can you talk -- can you share any thoughts regarding your partners' launch preparedness for roxa in the U.S. and/or preparations ahead of any FDA interactions like an Adcom?

Enrique A. Conterno

CEO & Director

Yes. So I -- clearly, the U.S. is the most important market, and we are treating it as such. And yes, I think AstraZeneca is leading much of our commercial preparations. And FibroGen does have an important role,

and I'll speak to that to ensure that we can be as ready and as prepared to be -- truly realize the promise that roxadustat has to be a transformational medicine in CKD anemia.

First, I think -- right now, I think one of the critical elements that we have to work on is, of course, ensuring that we appropriately manage the regulatory process, questions from the FDA and so forth. I think as far as the Adcom, we have received no indication that there will be an Adcom or that an Adcom is planned. It's -- that could change, of course, at any time. But as of today, we have not received such indication. Now regardless of that, we continue to prepare as if we were going to have an Adcom. We need to be ready to ensure if there is an Adcom that we can have the best showing possible of all of our data and all the questions that may be asked.

One other element that is critical is really the overall publication strategy. And you will see a robust publication strategy this year, including a number of abstracts and presentations or presentations as part of ASN. That is a big important target for us. There will be some other medical forum where we release publications, but that is going to be key. And in particular, as we focus on the elements of differentiation that I described. Yes, generally, publication, but really relevant publications, ones that truly matter in terms of the relevance that this product could have in clinical practice.

Finally, as we launch, clearly, it is going to be key that we basically get the right reimbursement for the product and that we are establishing the value proposition for the product for roxadustat in the U.S. marketplace. And I'm delighted to see what I'm seeing from AstraZeneca. I had a chance to meet and review with the U.S. team the plans, and we are in good constant communication, not just at top level but throughout with the different teams. So I'm excited to see the prioritization importance that AstraZeneca is providing to roxadustat in -- as basically, we prepare for a U.S. launch after the PDUFA action data at the end of the year.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Got it. How important -- with ESAs, it's priced in a way that there's more value generated if more drug is consumed with roxa. It's obviously going to be doses that is titrated to the individual level, weight-based. So would you envision a pricing scheme that does capture more value if more drug is utilized and you're treating to higher target hemoglobin levels?

Enrique A. Conterno

CEO & Director

Yes. We are not discussing pricing strategy at this stage. I appreciate the question. As you know, that's probably -- that's not on either AstraZeneca's and FibroGen's best interest to be discussing that publicly at this stage. I think you will hear about our pricing once, basically, we launch the product. But you do raise an important point, which is, at the end, how do we think about the overall value of the product. And keep in mind that, of course, if we broke or reduce this MACE events and then send out a product that on -- a product that reduces transfusions, a product that has good predictable response when it comes to efficacy across many different patients, I think that product can provide significant value, both clinically and also from an economic perspective to the health care system.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Yes. Now whether an Adcom is scheduled or not scheduled, I appreciate the comment that the expectation probably is that it doesn't. So from your perspective, does this have any read-through at all, perhaps how the FDA may be thinking about safety? I know there's a lot of investor focus regarding how safety risk, particularly CV safety risk, ultimately gets characterized to the class relative to the ESA category?

Enrique A. Conterno

CEO & Director

Yes. I -- honestly, I don't think about it that way. It's -- I think it's always not wise to speculate on how the FDA is thinking about something. Keep in mind that an Adcom is typically established to try to get

external feedback on whether it's approvability or a particular labeling or the risk-benefit on a particular subset of the population. So there are a number of reasons why an Adcom could be -- come to life and be called for. But I am quite confident that the FDA, given the data set that we have put forward, will -- based on the data, I think, will have a chance to have the appropriate review and come to all of the right conclusions in terms of the benefit risk profile of the product. Now that doesn't mean that they have an Adcom or not. It's -- and I don't see an Adcom or the lack of as a positive or negative. It's just part of the process.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Got it. Okay. Look, maybe we can just jump ahead to the China launch and the update provided on the 1Q update where I thought that the sales and the commentary around the hospital listing seemed generally positive. It seems like the tone or the messaging regarding the further ramp up in revenue, in this marketplace where you guys would seemingly have at least a 3- or 4-year lead head start versus your competitors, who I think have to satisfy a lengthy clinical burden to get to market. So can you talk a little bit about the -- what you're seeing in China at the moment? And what gets you excited about this market opportunity?

Enrique A. Conterno

CEO & Director

Clearly, I think -- I do. I think I'm excited in that we basically had about \$5 million -- we had \$5 million in net roxadustat revenues in China in Q1. This is the first quarter when we had posted the NRDL. So it's an important quarter to look at. But also, we need to keep in mind that this was a quarter where China was largely under lockdown for much of the quarter, at least 2 of the 3 months. We basically had COVID-19, basically, impacting hospitals, patient visits and so forth. And I think what I've commented on is not just the \$5 million and the fact that we expect a meaningful ramp up in revenue over the next few quarters. But the fact that we are -- we ended with listing that basically represent over 30% of the overall China opportunity. That's -- and this is across both DD and NDD. So I had the opportunity to manage China for Lilly, so I have some experience. And I can say that this is a very meaningful ramp up in terms of access to hospitals for any product. So when I look at hospital adoption, when I look at the adoptions or hospital listing, and when I look at the adoption of the product, the uses of the product within those hospitals, I really like what I see. And I think it gives me confidence, not just for China, but I think what this product would do everywhere else, right? It's very exciting to see.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Yes. How do you think about the pace of hospital listings going forward through the remainder of the year? I think you said you're at 30% right now. And even that, in and of itself, I think you guys have characterized it as pretty unprecedented. I think the U.S. investors generally haven't had to analyze in great level of depth or had great visibility into how the processes work in China. It's very unusual that we analyze the China launch first. So can you help us think about how this evolved?

Enrique A. Conterno

CEO & Director

It does. I think you can look at a number of benchmarks of products that have become blockbusters in China. And when I look at the uptick that we have in terms of listings and access to the overall opportunity, and I will put in parts, despite the fact that we had COVID-19 in the first quarter, I do think it is unprecedented. I expect that the listings and the uptick in listing will continue. So we're not commenting on at this stage, but we intend to provide another comment -- some more commentary at the end of, of course, Q2, both net product sales and listings. But I think what I basically see is that I'm highly encouraged with -- both what we have achieved and also the continuous trends that we basically see in terms of use of the product and listing adoption. One of the...

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

When you talk about blockbusters in China, are we talking about old drugs like lipitor that were well beyond their western market patent life that hit \$1 billion threshold? Are you talking about more innovative therapies and how those progress?

Enrique A. Conterno

CEO & Director

Yes. I'm really speaking -- I -- given that the NRDL has evolved over the years and provinces adopt reimbursement much quicker than in the past, it's not always fair to just look back and -- but I think you can look at our products today, in some cases, the products are -- they're early in their life cycle and to try to see what is it that they have achieved when it comes to hospital listings. So I'm really thinking of innovative therapies and what is the ramp up. So yes. I -- honestly, if you go back, and I'm going to go back a few years, but you go back 5, 6 years, to get meaningful reimbursement, both reimbursement on hospital leases in China, it used to be a process that used to take years, 4, 5, 6 years, before you had meaningful listings, meaningful reimbursement.

So we are 1 quarter post the NRDL, and we are -- we feel very good about the support that we're getting, the use. And something that I commented on the call briefly was that, importantly, we are seeing use across very different segments, which I think is very important, which is -- because I think it tells you something about the ability to scale these products, whether it's in dialysis centers, whether it's in home dialysis or whether it's in nondependent dialysis. So we've seen uptick across. Of course, we need more data to look at a number of additional parameters, whether it's what's the source of this patient, were these patients naive to therapy, were they on ESA before. So that color, I think we'll be able to provide sometime in the future as we get more and more substantive data. But I think what we basically have seen right now is good use, broad use across all of the segments that we're interested in.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

And from a safety labeling perspective in China, can you talk about how it's conveyed or communicated to health care providers, the safety profile relative to ESAs, because one unique aspect of this is that you're doing your MACE outcome trials in this population on a post-market basis?

Enrique A. Conterno

CEO & Director

Yes. So keep in mind that ESAs in China do have a black box, and we do not. So our -- the product profile in China includes, of course, some of the efficacy profile, some of the safety elements, but it does not include, I think as you allude to, all of the pooled safety data from all of our trials and so forth. Clearly, that's -- as we get approval in the U.S., and over time, I expect that more data will be added to our Chinese label. It's difficult to say when will that happen. But right now I think it's the -- I think if I understood your question, our label does not include a black box.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Yes. Okay. Fair enough. And there has been some recent focus from investors regarding competitors in the HIF class. So with data recently released in the dialysis setting, maybe you had mentioned roxa on hemoglobin response being superior. Just wondering how much of that was driven by potentially trial design differences? For example, differences in dosing algorithms and target hemoglobins and the ability to use different rescue treatments. Wondering how one can make that cross-trial inference that maybe one agent might be more affected than another.

Enrique A. Conterno

CEO & Director

Yes. I think if you're -- so let me make a comment on -- which I think is a great opportunity. Anytime a competitor releases data, I think it does a few things. First, I think in this particular case, it reinforces the -- further reinforces the overall HIF-PHI class, okay? But I think it's also an opportunity to highlight

why roxadustat and why I'm so encouraged about roxadustat. And keep in mind that roxadustat, as I mentioned, when it comes to hemoglobin in DD, we basically showed statistical superiority versus EPO. Clearly, that's -- and hemoglobin is something that basically translates to transfusion rates, lower transfusion rates, better achievement of hemoglobin target. So I find that to be a very compelling metric. Now that's something that we have shared, which is that we have lower transfusion rates than EPO. Of course, lower transfusion rates in the case of NDD relative to placebo, but that is an outcome that is very important. I also talked about incident dialysis and the data that we have there. Given that, that is a natural decision point, I feel that our data basically puts us in a different category from any therapy at this stage to be able to raise the needs of those patients. So I really like the hand that we have there. It's a hand that is, I believe, is highly differentiated. And now with the data from our competitor, in a certain way, validates that class, but at the same time it, I think, further highlights the elements of differentiation that are meaningful that we basically we have.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Got it. Great. Well, Enrique, we are up against our time. So I want to thank you so much for joining us and sharing your insights on the latest developments at FibroGen. So thank you very much.

Enrique A. Conterno

CEO & Director

Thank you very much, Jason. It's been a pleasure.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

All right. Well, with that, have a good day, Enrique. And operator, we can conclude the call.

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EXHIBIT Z

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EDITED TRANSCRIPT

FibroGen Inc at Jefferies Healthcare Conference (Virtual)

EVENT DATE/TIME: JUNE 02, 2020 / 7:30PM GMT

CORPORATE PARTICIPANTS

Enrique Conterno FibroGen, Inc. - CEO

CONFERENCE CALL PARTICIPANTS

Michael Yee Jefferies LLC - Analyst

PRESENTATION

Michael Yee Jefferies LLC - Analyst

Hey, everybody, welcome to another afternoon session at the 2020 Jefferies Global Healthcare conference. It has been a fantastic success so far. And up next with us this afternoon I'm really happy to see the CEO of FibroGen, Enrique Conterno, on the line with us there from San Francisco.

Enrique, congrats on all the progress so far since you joined on, I guess end of 2019, and really started to meet everybody at the beginning of 2020 as sort of a big coming out year for you.

Maybe -- I'll turn it over to you. Maybe just give us a brief comment on how things have evolved for you at FibroGen as you have come on. And what are the most important things you're focused on executing on this year? And give us a little bit of context of what's going on at FibroGen right now. And then we're going to go into some of the details, obviously, with a lot of things coming up.

Enrique Conterno FibroGen, Inc. - CEO

Very good. Thank you very much, Michael, for the invitation. I think our priorities here at FibroGen are pretty clear. We have a compelling value proposition with roxadustat, a transformational medicine for anemia. We are of course first pursuing that in CKD anemia, but we're also pursuing additional indications. Regulatory success, the publication plan, planning for reimbursement are all critical for us.

We are very much focused on accelerating the enrollment of pamrevlumab across the three high-value indications that we are pursuing starting with IPF, also LAPC and also Duchenne muscular dystrophy. And as we've related recently, we are also pursuing a couple of COVID trials, which I think can be important and meaningful.

Now finally, leveraging the scientific platforms that we have to bring new products into the clinic. Those are the [priorities] that guide us and I'm very pleased with the progress that we continue to make.

Michael Yee Jefferies LLC - Analyst

That's fantastic. So, you do have a lot on the plate, Enrique, because -- just in brief, you of course were trying to execute on roxa. That's usually the most important; I will get into that. You're trying to execute on pamrevlumab and trying to get that enrolled obviously, which is important.

So, maybe just starting with roxa, you've reported out all the data last year at ASN. You've submitted the NDA, you were accepted in a standard review. You're coming up on your mid-cycle review meeting. Maybe talk with us about how the interactions with the agency have been going.

Peony used to say they were very excited to get that application underway, no issues with that. There's always been a lot of investor controversy around the package and everything. Maybe just talk about how those interactions have been going, even during a COVID environment, of course, and an upcoming mid-cycle review and how you're feeling about this.

Enrique Conterno FibroGen, Inc. - CEO

We are feeling good about the engagement we have with the FDA. As you know, we have a PDUFA date for December 20 of this year. As you well point out, we do have the mid-cycle review coming up, it has been scheduled for now for the month of June, so this month.



We are basically fully engaged and making sure that we are addressing any questions the FDA has and continue to make progress in this review. I think this is critical for us, not only that we get approval, a broad approval, but importantly that we have a very good label.

Michael Yee Jefferies LLC - Analyst

Right. So, digging into that a little bit, you've previously said you do expect at least to get more color on whether or not there's going to be a panel. And mid-cycle reviews, if you look at FDA documents, typically they say you should get a much better picture about that. Is that something you would eventually disclose? How are you feeling about a panel? Would you tell us when you know or wait for an earnings call? That's question one.

And then question two is between now and the PDUFA, what are the gating steps towards getting approved? Is that a factory inspection, manufacturing inspection and launching preparation to help out AstraZeneca? Maybe just talk to between June and December.

Enrique Conterno FibroGen, Inc. - CEO

So, as we have shared in the past, when it comes to an Adcom, typically the FDA communicates a sponsor and this should be planning for an Adcom either pre-submission or during filing acceptance. We have no indication of an Adcom at either those events or now at this stage.

Clearly the mid-cycle review is the last time really where the FDA would typically let us sponsor -- know that an Adcom is coming. Not that it could not happen after that, but clearly the likelihood of it happening decreases substantially after the mid-cycle review.

There are a number of elements that we go through a review which include, like you say, preapproval inspections and so forth. I think the mid-cycle review I think is very informative because, in a certain way at that point, we are basically discussing the overall status of the application with the FDA including any findings that they may have, any issues.

You also, importantly, discuss at the meeting, as you know -- you start a high level discussion around labeling. And finally, I think it is specifically stated that it is also a meeting where you basically finally determining whether an Adcom would be held or not. So, a confirmation or not of whether there's going to be an Adcom.

So, a number of things we are looking forward as we prepare for that meeting. Clearly there is a mid-cycle review. There's a late-cycle review as well, which we expect will happen in September. And then I think at the end you end up being in labeling discussions, which basically that happen in much more detail within the last 30 days.

Michael Yee Jefferies LLC - Analyst

And would you disclose -- if they told you there was a panel would you wait for earnings? And how much is AstraZeneca involved in this? Because you actually I think own the actual NDA. But is a lot of this joint with Astra just in terms of FDA meetings and all that kind of stuff? How does that work?

Enrique Conterno FibroGen, Inc. - CEO

Yes, so we basically are the ones that are leading some of the discussions -- the engagement with the FDA. But of course we are preparing with AZ together to ensure that we have the very best thinking when it comes to ensuring that we can achieve regulatory success.

So, it is truly a joint effort. But we are right now the NDA holders. So, that's where we are. In terms of whether -- if the FDA were to tell us about an Adcom and that we should plan for one, yes, that's something we would plan to disclose. And ideally I think right away after we know.

Michael Yee Jefferies LLC - Analyst

Right away, okay. Fantastic. As you get towards thinking about approval and label, as obviously you are preparing for, what is the perfect label? What is a label you'd like that's for the treatment of anemia in both a CKD dialysis population as well as a non-dialysis population?



What does that look like in terms of the exact indication filed for?

And how do you think about the pluses and minuses about whether they would actually put a black box on that given that it's not the same mechanism as Epogen, right? So, even though it stimulates the production of hemoglobin, it's not the exact same mechanism.

So, given your experience in this field having spent a long time at Lilly blending through these different programs in diabetes, talk to us about how those things are weighed in terms of black boxes. Because I think there's examples in diabetes where some drugs in the same class do and don't, and that's in the same mechanism. Correct me if I'm wrong, Enrique. So, maybe just talk to the label in terms of indications and then how you think about how the FDA thinks about black boxes.

Enrique Conterno FibroGen, Inc. - CEO

Yes, I think -- given the data that we have, I think we warrant a label that is broad both in dialysis and NDD, a label that basically speaks to the safety of the product when it comes to cardiovascular safety. Of course only efficacy that we basically have and, in particular, the fact that we are able to reduce transfusions, which is an intended goal of treating anemia. And we did that -- we did so relative to Epogen in dialysis dependent --.

Michael Yee Jefferies LLC - Analyst

Is that something that can make a label though, Enrique? Is that something that would make a label? These are secondary endpoints.

Enrique Conterno FibroGen, Inc. - CEO

Yes, it is -- the question is -- you are asking when it comes to the label -- clearly this is a secondary endpoint that was included in all of our trials. And the question is in what way is this going to be included or what level of claim can we make I think. So, is it going to be reported as far as the clinical trials in the label? I believe so. What level of claim can we make? And --.

Michael Yee Jefferies LLC - Analyst

Like it would be in the efficacy table, you think that kind of stuff would be in an efficacy table?

Enrique Conterno FibroGen, Inc. - CEO

It could be, not as a primary outcome. As you know, it's clearly -- it is around increasing hemoglobin. And then I think, similarly to that, I think it's important that we get the incident and dialysis data on the label.

Similar to the comment that you were making, it's not like we are going to necessarily an indication around reducing the risk of MACE in incident dialysis. But I do believe that we -- that data warrants(inaudible) for this to be included in the label when we look at the observation what we observed in that population.

Michael Yee Jefferies LLC - Analyst

So, tie that into how the agency thinks about the various scenarios with the black box. Because the idea of having a cardiovascular benefit in the incident dialysis population, an important population but a sub-segment of CKD dialysis. Do they let you put in that Kaplan-Meier curve? I don't know what secondary endpoints are allowed to go into --.

Enrique Conterno FibroGen, Inc. - CEO

So, clearly we -- let's look at the two segments. I think in NDD we basically have a comparison relative to placebo. And therefore when we look at our data, I feel it basically shows that the product is safe, because of the safety profile when it comes to CV comparable to placebo.

In DD, yes, the question could be raised, well, you're comparing yourself to a product that has a black box in DD, and I get that. But in DD, when it comes to incident dialysis, we do show an actual significant benefit with a 30% reduction in MACE. When I put those two reasons together and look at the compelling nature of our data, I feel that the data does not warrant a black box related to CV Safety.



Michael Yee Jefferies LLC - Analyst

Those are two important points. One is you against placebo non-dialysis and you're non-inferior to a placebo. And two is, in a big sub-segment you are actually superior.

Enrique Conterno FibroGen, Inc. - CEO

Correct.

Michael Yee Jefferies LLC - Analyst

And if you go back and look at even drugs in diabetes, are there examples where one had a black box for some issue and others did not even within the same class? Is that possible?

Enrique Conterno FibroGen, Inc. - CEO

It is possible and there are (inaudible). Let's keep in mind we are not the same class even as EPO of course. We are a HIF PHI, so it is a new class. But you do have examples. The FDA tends to make decisions based on the data that is in front of them. And you have classes in diabetes, for example, where different products belong to the same class, some have a black box and some do not.

You can see it in the SGLT2 class and you can see it in the [GLP1s]. So, both important, key leading growth classes where you have the differentiation. Even though products belong to the same class, they do have different relative labels.

Michael Yee Jefferies LLC - Analyst

Perfect. Okay great, great. And then, so once we get all this -- we'll get the label, we'll review it. I'm sure you're very excited about launch. Typically Wall Street says, well look, launches are always tough.

Is this something where you would feel very good about a launch and it would be atypical versus other historical renal launches because maybe it's not in the bundle or maybe there's other reasons? Maybe talk about the push and pull with a launch in a renal setting where, again, Wall Street has been disappointed on renal launches.

Enrique Conterno FibroGen, Inc. - CEO

Well, one has to look at the benefits of the product. And I do view this product as a transformation product for anemia. If you are thinking of dialysis and if somebody is starting dialysis, with the type of benefit that we're showing in incident dialysis, this product should become standard of care.

Now there are mechanisms today due to TDAPA, for example, to be able to ensure that there is an incentive for dialysis organizations to include innovation into their protocols and to do so quickly. As you know as part of TDAPA, that's a decision we'll receive an add-on payment for including this innovation for a period of two years. So, this add-on payment is over and above the bundle and is -- basically that payment is at the level of 100% of the ASP.

So, it is an important factor that CMS and those guidelines to ensure that innovation is brought into the standard of care when treating patients with dialysis.

Michael Yee Jefferies LLC - Analyst

So, the treatment of anemia in CKD is in a dialysis bundle, but here there could be an add-on payment to reimburse users of new technology to offset that. That's the point.

Enrique Conterno FibroGen, Inc. - CEO

That is correct.

Michael Yee Jefferies LLC - Analyst

Why, I'm not sure that the terminology -- people say not in the bundle per se means that it's not a cost. I mean, it's not like it's an outpatient, you see what I'm saying, where they --?



Enrique Conterno FibroGen, Inc. - CEO

Yes.

Michael Yee Jefferies LLC - Analyst

Okay, all right. I think that's fair. Okay, so that's really important if that happens. And you feel very confident that that would be in the TDAPA add-on?

Enrique Conterno FibroGen, Inc. - CEO

I feel that should be the best case. Of course, we had discussions with CMS and we do believe that roxa is eligible. And we are planning to apply as soon as we get approval.

Michael Yee Jefferies LLC - Analyst

Okay, great. Alright, so hopefully that's a positive dynamic. Now there's also some interesting data points already, Enrique, because you have a launch in China. You were appointed \$5 million in the first quarter during a COVID environment in China. I don't think anyone is calling victory yet on \$5 million.

But talk to what you are seeing in China as at least some read through. Is \$5 million good? What happens in the second and third quarters? Because China is kind of obviously not so much in shelter-in-place, and how do you think about the value there in China that you are seeing?

Enrique Conterno FibroGen, Inc. - CEO

I think it is significant and I think it is giving us a lot of confidence about -- given the adoption that the product has. When we look at the \$5 million, yes, it's \$5 million, but it's the first quarter both reimbursement. And keep in mind that that quarter was a quarter where, in China, for two out of the three months we basically had a complete lockdown of the country, so very little activity.

One of the leading indicators that we look at in China is basically how are we doing when it comes to hospital listings. Because you get national reimbursement, but for the product to be prescribed in a hospital, then you need to be listed in that particular hospital. And we are doing, I believe, exceptionally well.

And I look at and benchmark roxadustat to what I'm going to call blockbuster products in terms of achieving hospital listings. And we are benchmarking extremely well relative to any blockbusters that we will benchmark against.

So, for example, after the first quarter we were basically accessing based on the hospital listings we had already over 30% of the anemia market for CKD in China across both DD and NDD. That is very significant for three months. And keep in mind that in that period we had once again a lockdown.

So, what we've seen in China is a significant level of activity post that across not just promotion activity but also hospital listing activity and adoption. So, we expect and, as I mentioned -- as I mentioned, Michael, we expect a significant ramp-up in revenues in the next quarters.

Michael Yee Jefferies LLC - Analyst

Walk me off this math, Enrique, because it was shut down for essentially two out of three months. You did \$5 million and you only have 30% of the hospitals on formulary. Now maybe those are the biggest 30% -- 30% of the numbers, but those are the biggest ones. I don't know it it's -- they're not obviously all equivalent. But is that focused on the bigger ones? So, I don't want to read in just saying, oh, just 30%, gross it up.

Enrique Conterno FibroGen, Inc. - CEO

The 30% represents of the overall opportunity. If you look at number of hospitals it's less than that, but the hospitals represent 30% of the overall.



Michael Yee Jefferies LLC - Analyst

Yes, so you're penetrated 30% of the opportunity on the formulary side and there is already \$5 million okay. And a significant uptake is what you said (multiple speakers).

Enrique Conterno FibroGen, Inc. - CEO

Yes. And for all the reasons that you describe is we feel very good. And there are a number of qualitative elements as well that make us feel good about our uptake there, including the fact that we see use that is not just tailored or focused on one segment.

We basically see use across very different segments that give me the perspective that we have many different ways of growing, many different levers to grow longer-term, including we've seen significant use in NDD, which is going to be immensely important in China.

Michael Yee Jefferies LLC - Analyst

So, there were some NDD sales already in that \$5 million?

Enrique Conterno FibroGen, Inc. - CEO

That is correct.

Michael Yee Jefferies LLC - Analyst

Okay. Last question before I get into some other topics, historically the management and the Board of FibroGen has suggested that China value is underappreciated and you wanted to get national reimbursement and all these other things. Is that still something you would think about in terms of an untapped value doing something? Or is there still stuff you just want to get done with first and we'll talk about it down the road type of thing?

Enrique Conterno FibroGen, Inc. - CEO

Yes, It's a good question. I do believe that the China values and the opportunity there is under-appreciated. That's something that we will provide some clarity down the road in terms of how we ensure we look at capitalizing, making sure that there is visibility to this very tangible value that we basically have given our operations there.

Right now for us at this particular time I think it's critical that we have the organization fully focused on the launch itself. Because -- given the prospect that we have, meaningful profit to build a major blockbuster in China, the optionality that provides for us is very significant in a number of different ways.

Michael Yee Jefferies LLC - Analyst

I mean think about that because there's almost a source of capital. If you were to spin that out or use it to raise capital and spin that. And I'm sure you can get great valuation for that given people would appreciate that and that's a source of capital for you if that was to happen.

Okay. Let me shift gears. Two other things possible, roxa and MDS. Just like with on that, do you think there's Phase 3 data in 2021 as well which could further expand the opportunity, [how] I should think about that? And how do you think about that versus say Acceleron's product. Or I guess it is Acceleron selling to Bristol?

Enrique Conterno FibroGen, Inc. - CEO

I do think that we are expecting that trial to be fully enrolled this year and be able to have some data next year. We do view this product as broader than the product that you are referring to. So we are able to access really a much broader opportunity when it comes to MDS.

We are also -- I do believe that one opportunity that's under-appreciated also is our chemo-induced anemia opportunity, because that's meaningfully even larger than MDS when we look at the opportunity size. And that trial, as you know, is in Phase 2, but we expect to start Phase 3 potentially next year, so it's very exciting for us.



Michael Yee Jefferies LLC - Analyst

Okay, that was a pretty meaningful proportion of EPO sales if you go back.

Enrique Conterno FibroGen, Inc. - CEO

It is and there's no reason why we have great data where we could not reestablish the treatment of anemia in a meaningful way in that setting for those patients.

Michael Yee Jefferies LLC - Analyst

Okay, great. And then in the last couple of minutes, shifting gears from all the value potential out of roxa -- Pamrevlumab, on one hand I feel like timelines are a little bit long because LAPC, or local advanced pancreatic cancer, for those listening, is enrolling. I don't think you've said it's completed enrollment.

And then on IPF there were some COVID delays there, so that's still getting underway. So, it feels like timelines are [wrong]. Do you still feel like you could have resection rate data in 2021?

Enrique Conterno FibroGen, Inc. - CEO

Yes, so we have not provided timelines when it comes to any of our programs at this stage. I think what we've shared is that we intend to provide specific timelines in the second half of this year when it comes to pamrevlumab on every single other program. Just maybe an update because we have a number of moving pieces here.

But when it comes to IPF, as you know, we had post-enrollment for that IPF trial given the vulnerability of those patients. I'm pleased to report that we are restarting enrollment on a side-by-side basis as we speak. So, that's happening as we speak.

Clearly for us I think site activation is key. That's expanding the number of sites in a dramatic way. I think it's critical to achieve the enrollment timelines that we need. And as part of that we are, of course, expanding into other countries including China where now we expect that we will be able to start enrollment this year in China [in IPF]. That's meaningfully important.

Michael Yee Jefferies LLC - Analyst

What about LAPC? That was never paused right? When would you complete enrollment there?

Enrique Conterno FibroGen, Inc. - CEO

So, once again, we haven't provided that. We intend to provide that timeline in the middle of the year, but that has not been paused. But we did see an impact as a result of COVID. We expect that as the pandemic will go to a somewhat new normal, that we will see a reacceleration.

We're also activating additional sites when it comes to LAPC. You correctly point out that we are looking at the resection rates as a surrogate for a meaningful clinical improvement. Because we know that with resection basically the likelihood of survival increases dramatically. We have a meaningful difference in the resection rate. We believe that we might be able to have accelerated approval for this product which would be very exciting.

Michael Yee Jefferies LLC - Analyst

Very good. I look forward to that data because that is important. And it's actually -- that shouldn't be a timeline long from completion to enrollment. Because obviously it's a rapidly progressing cancer. Enrique, thank you very much. We're on a tight schedule. You have a ton of other one-on-ones to get to. So, thank you for your time today. You look great and we look forward to the updates.

Enrique Conterno FibroGen, Inc. - CEO

Thank you so much, Michael.



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EXHIBIT AA

S&P Global
Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN Shareholder/Analyst Call

Thursday, June 04, 2020 4:00 PM GMT

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EXECUTIVES

Enrique A. Conterno CEO & Director

Michael D. Lowenstein Chief Legal Officer

Presentation

Operator

Good morning, and welcome to the 2020 Annual Meeting of Stockholders for FibroGen, Inc. I would now like to turn the conference over to Enrique Conterno, the CEO and Director of FibroGen. Please go ahead.

Enrique A. Conterno

CEO & Director

Thank you and good morning. I'm very happy to welcome everyone to the FibroGen 2020 Annual Meeting of Stockholders. At the request of the Chairperson of our Board, Jim Schoeneck, I will act as Chairman of this meeting. Normally, our annual meetings are held in person, but due to the COVID-19 pandemic, this year's annual stockholder meeting is being held online for the first time in a virtual telecast format to protect the health and well-being of our stockholders, Board of Directors and employees.

Since this is the first virtual annual meeting we have conducted, please bear with us if we encounter any technical issues. Before I call the meeting to order, I would like to take a moment to recognize and thank Dr. Toshinari Tamura for serving on our Board of Directors for 11 years. Dr. Tamura joined the Board following his tenure as a Senior Executive at Astellas, where he was instrumental in developing and managing the partnership with FibroGen. And he has provided outstanding counsel and guidance as a Director of FibroGen, in addition to his invaluable service as a member of our Scientific Advisory Board. As a partner, as a director and as an adviser, Dr. Tamura's contributions to FibroGen have been significant, and we are deeply appreciative. We thank him and wish him well.

I would like to introduce the members of the Board and Executive Committee management, who are with us today. All of our members of the Board are here today, Jim Schoeneck, Chairman of the Board; Suzanne Blaug, Jeffrey Edwards; Jeffrey Henderson; Dr. Maykin Ho, Thomas Kearns Jr., Dr. Kalevi Kurkijärvi, Gerald Lema, Rory Riggs; and Dr. Roberto Pedro Rosenkranz. The other officers of FibroGen here today are Pat Cotroneo, Chief Financial Officer; Rod Fuhriman, Vice President and Controller; and Michael Tung, Vice President, Investor Relations and Corporate Strategy. Please let me also introduce Michael Lowenstein, Chief Legal Officer, who will act as secretary and inspector of elections of this meeting. I would also like to introduce Greg Vlahos of PricewaterhouseCoopers, FibroGen's auditors, who is available to respond to appropriate questions.

Before turning to the formal business of the meeting, I would also like to mention some procedural matters that are different this year due to the online format of the stockholder meeting. First, there is an agenda outlining the components of this meeting, which should be visible in the top right corner of the online portal for this meeting. Second, the stockholders of FibroGen as of April 9, 2020, record date, are able to vote during this meeting, until we close the polls following the presentation of the proposals.

You may vote by clicking on the Vote Here button on the bottom-right portion of the website page for this meeting. If a stockholder has already voted online by telephone or mailing a physical proxy card, voting at this meeting is not necessary. However, a vote submitted at this meeting will supersede an earlier vote. Third, questions pertaining to the business of this meeting may be submitted by stockholders during the meeting in the Ask a Question Box, on bottom-left portion on the online portal for this meeting. [Operator Instructions] Fourth, we are recording this meeting, and you'll be able to replay the recording for 30 days from the website page for this meeting. Please wait a day or so after this meeting for the recording to be uploaded.

The meeting is now -- the time is now 8:06 Pacific time on Thursday, June 4, 2020, and meeting will now officially come to order.

We propose to proceed with a formal business of the meeting as set forth in your notice of annual meeting and proxy statements, and we will address questions pertaining to the business of today's meeting that are submitted through the online portal for this meeting. After the formal part of the meeting, I will give a brief update presentation on the company.

Will the secretary please report, at this time, with respect to the mailing of the notice of the meeting and the stockholders' list.

Michael D. Lowenstein

Chief Legal Officer

I have at this meeting a complete list of the stockholders of record of FibroGen's common stock on April 9, 2020, the record date for this meeting, and a list of the registered holders is available on the virtual meeting website. I also have with me an affidavit certifying that on or about April 23, 2020, a notice of Annual Meeting of Stockholders of FibroGen was sent to all stockholders of record as of the close of business on April 9, 2020.

Enrique A. Conterno

CEO & Director

Mr. Lowenstein has been appointed by the Board to act as inspector of elections at this meeting and has taken and subscribed the customary oath of office to execute his duties with strict impartiality, which will be filed with the records of the meeting. His function is to decide upon the qualifications of voters, accept their votes and to tally the final votes.

Will the secretary please report at this time with respect to the existence of a quorum?

Michael D. Lowenstein

Chief Legal Officer

Proxies have been received for 78,413,546 of the 89,068,759 shares of common stock outstanding on the record date, which represents approximately 88.03% of the total number of outstanding shares. This constitutes a quorum for the meeting today, and we may now carry out the official business of the meeting.

Enrique A. Conterno

CEO & Director

Very good. We will now proceed with the formal business of this meeting. There are 3 proposals to be considered by the stockholders at this meeting. The first item of business today is the election of our 4 Class III Director nominees, Thomas Kearns, Dr. Kalevi Kurkijärvi, Gerald Lema and myself, to the Board to hold office until the 2023 Annual Meeting of Stockholders or until their successors are elected.

The second item of business today is the approval on an advisory basis of the compensation of FibroGen's named executive officers as disclosed in the company's 2020 proxy statement.

The third item of business today the ratification of the selection of PricewaterhouseCoopers by the Audit Committee of the Board of Directors as the independent registered public accounting firm of FibroGen for the year ending December 31, 2020.

That was the final proposal for today's meeting. The secretary will now describe the voting procedures.

Michael D. Lowenstein

Chief Legal Officer

Each share of common stock is entitled to 1 vote. Voting is by proxy, telephone and mail prior to the annual meeting and by proxy online at www.virtualshareholdermeeting.com/fgen2020 during the annual meeting. You do not need to vote on the virtual meeting website if you have already voted your proxy online, by telephone or by mail. The time is now 8:11 and the polls are now closed for voting.

My report as inspector of elections covering the proposals presented at this meeting is as follows: the proposal to elect our Class III Director nominees, Enrique Conterno, Thomas F. Kearns Jr., Dr. Kalevi Kurkijärvi and Gerald Lema to the Board, is carried with each director receiving the votes of the holders of at least 94.5% of the shares voting.

The proposal to approve, on an advisory basis, the compensation of FibroGen's named Executive Officers as disclosed in the company's 2020 proxy statement has passed with 63,834,655 voting in favor; 816,731, opposed; and 127,652 abstaining.

The selection of PricewaterhouseCoopers by the Audit Committee of the Board of Directors as the independent registered public accounting firm of FibroGen for the year ending December 31, 2020, has been ratified with 77,823,779 voting in favor; 308,758, opposed; and 281,009, abstaining.

We expect to report our preliminary voting results, or if available to us on a timely basis, our final voting results on a current report on Form 8-K to be filed with the SEC within 4 business days after the end of this meeting. If not earlier reported, we expect to report our final voting results in an amendment to our Form 8-K within 4 business days after the final results are known to us.

Enrique A. Conterno

CEO & Director

This concludes the formal portion of today's meeting. We now adjourn the meeting before proceeding to the corporate presentation.

So I would like to wrap today's meeting with a brief presentation about company business. I would like to remind everyone that this presentation contains forward-looking statements that involve substantial risks and uncertainties. Including those described in the Risk Factors section of our most recent quarterly report on Form 10-Q.

Let's start with a brief company overview. First, it is important to reinforce our commitment to our mission, developing innovative, first-in-class medicine for the treatment of chronic and life-threatening or debilitating conditions. And our goal is to deliver value to both patients and shareholders. We have established 3 broad goals: first, ensuring the regulatory and commercial success of roxadustat, a transformational medicine in anemia therapy, first applied to treatments of patients with chronic kidney disease with significant potential for expansion into treatment of other anemias. Second, accelerating the development of pamrevlumab in our 3 high-value indications of idiopathic pulmonary fibrosis, locally advanced and resectable pancreatic cancer and Duchenne muscular dystrophy. And third, reenergizing our research agenda by delivering on our unique scientific expertise of both hypoxia-inducible factor, or HIF, and connective tissue growth factor, or CTGF biology to create a rich and broad pipeline of next-generation drug candidates.

Our financial position is strong with approximately \$600 million in cash at the end of the first quarter. We have a total of \$375 million in anticipated milestones expected through mid-2021, including the \$130 million in milestone for the European filing we just earned, plus \$245 million of milestones on U.S. and EU approvals and first commercial sale.

Based on our current forecast, we expect our estimated 2020 ending cash to be in the range of \$720 million to \$730 million, and we believe we're well financed for years to come.

Let me begin with roxadustat's first-in-class product program. In anemia associated with chronic kidney disease, or CKD, roxadustat was first launched in China. I will cover this exciting launch in more detail later in the presentation. Roxadustat has also been launched in Japan for the treatment of dialysis-dependent patients, and the supplemental new drug application for non-dialysis-dependent patient was submitted in January. In the U.S., the FDA is actively reviewing our roxadustat new drug application for both dialysis-dependent and non-dialysis-dependent patients and has set a PDUFA date of December 20, 2020.

In May, the roxadustat marketing authorization application for both dialysis-dependent and non-dialysis-dependent patients was accepted for review by the European Medicines Agency. Finally, there have been additional roxadustat submissions in a number of countries, including Canada, Mexico, Australia and South Korea, to name a few.

Beyond chronic kidney disease, our vision is for roxadustat to become the standard of care for anemia broadly. We continue to develop roxadustat for the treatment of anemia associated with myelodysplastic

syndrome, or MDS, which is in Phase III, and in chemotherapy-induced anemia, or CIA, which is in Phase II.

Moving now to pamrevlumab, our first-in-class antibody that inhibits the activity of connective tissue growth factor, or CTGF, a common factor in fibrotic and proliferative disorders.

First, on our important IPF program, given the recent COVID-19 pandemic, we had previously announced a pause in the enrollment of our ZEPHYRUS Phase III trial to ensure patient safety in this vulnerable population with compromised lung function. Working closely with clinical investigators of sites, we have now restarted enrollment of ZEPHYRUS and are on track to initiate ZEPHYRUS 2, our second pivotal Phase III trial in IPF later this year.

LAPIS, our ongoing Phase III trial in locally advanced and resectable pancreatic cancer, or LAPC, continues to enroll. Finally, we continue to prepare to initiate a Phase III trial, LELANTOS, evaluating pamrevlumab as a treatment for Duchenne muscular dystrophy, or DMD, in the third quarter of 2020.

As you can see from this slide, FibroGen has a robust late-stage pipeline. We are committed to accelerate in the development and rates of clinical trial enrollment across all of our programs. One of the areas that I have been impressed with joining FibroGen is the level of understanding that we have when it comes to both HIF and CTGF factor biology. If biology is involved in a number of different critical metabolic and regulatory processes in the body and provides unique opportunities to target a variety of diseases. Similarly, there are multiple potential application for CTGF biology in fibrosis and oncology.

FibroGen has one of, if not the largest, libraries of HIF and CTGF compounds allowing us to potentially target a plethora of therapeutic patients.

When speaking about research, the aim here is very clear. It is to develop new drug candidates to ensure and provide a sustainable stream of innovation based on these 2 scientific platforms. We will be providing more details on our earlier research programs, scientific agenda and development time lines in the second half of this year.

Now I would like to review roxadustat's highly differentiated efficacy. Roxadustat is the only HIF prolyl hydroxylase inhibitor to date to demonstrate superior efficacy versus epoetin alfa and placebo in the dialysis-dependent and non-dialysis-dependent patient populations' perspective. There is a direct correlation between hemoglobin level and the rate of red blood cells transfusion. And roxadustat has demonstrated a statistically significant reduction, the risk of transfusion in both that the dialysis-dependent and non-dialysis-dependent patient populations.

Clinical outcomes are extremely relevant to patients, physicians and payers. Additional benefits of roxadustat in the dialysis patient population include the fact that patients on roxadustat require less IV iron and roxadustat is effective in treating patients with inflammation.

Importantly, CV safety was demonstrated across all studied populations. Non-dialysis-dependent, incident dialysis and dialysis dependent. Today, I'd like to highlight the incident dialysis patient population. Let's start first with some definitions. Incident dialysis patients are those patients who are within 4 months of initiating dialysis for the first time. Time to -- the first major adverse cardiovascular event, or MACE, is a composite endpoints for all-cause mortality, myocardial infarction and stroke. And time to first MACE+ is a composite endpoint, which includes MACE events as well as unstable angina and heart failure requiring hospitalization.

In incident dialysis patients, roxadustat reduced risk of major adverse cardiovascular events or MACE by 30%. And reduce the risk of MACE+ by 34% compared to epoetin alfa. Both results were statistically significant. There was also a trend towards lower all-cause mortality relative to epoetin alfa. Roxadustat clearly provides a large clinical benefit in the incident dialysis patient population, and we believe this is a natural decision point for health care professional when selecting which therapeutic agent will be utilized in the treatment of anemia. This is highly relevant. As in the U.S., 86% of dialysis patients do not start today anemia therapy until the incident dialysis period. Said another way, only 14% of patients have been exposed to an ESA in the 12 months prior to initiating dialysis.

Some of you may have heard the term pipeline in a product. Next slide, please. And I think this slide illustrates the different anemias in which roxadustat could potentially play a role. We're well on our way to addressing the anemia of chronic kidney disease opportunity. But anemia associated with secondary chronic kidney disease, cancer and inflammation are all large unmet medical needs. We and our partners are committed to making roxadustat the standard of care when treating anemia regardless of the etiology of the disease, and this provides a good transition to the next slide.

FibroGen has in place 2 important roxadustat partnerships, 1 with AstraZeneca and 1 with Astellas. As of the end of the first quarter of 2020, FibroGen had received over \$1 billion total from these 2 partners since the start of the partnerships, made up of approximately \$750 million in upfront payments and approximately \$250 million in development and regulatory milestones. Still to come are approximately \$1.5 billion in outstanding potential milestones, \$375 million of which are expected by mid-2021.

This \$375 million in near-term milestones can be broken down into \$130 million on EMA submission, which we have just earned. And \$245 million on U.S. and EU approvals and first commercial sale.

In addition, we received our royalty and our transfer price in the low to mid-20% range in the U.S., Europe and rest of the world territories, except in China, where there is a 50-50 profit split.

Finally, we received full partner reimbursement for both the development and commercialization of roxadustat in all geographies, except in China. Where we share these expenses 50-50 with AstraZeneca.

Returning to China. As you know, the first regulatory approval for roxadustat was in China and roxadustat was included in the national drug reimbursement list, or NRDL, which went into effect at the beginning of the year. The launch is going very well. And in the first quarter of 2020, we reported \$5 million in net roxadustat revenues despite much of the country being locked down due to COVID-19. A key focus in China has been and continues to be expanding hospital listings, so the roxadustat can be widely prescribed. And the hospital where we are listed as of the end of Q1 represent 30% of the CKD anemia market opportunity, which is great progress. As we stand here today, we have seen a steady return to a new normal in China, and we expect a meaningful ramp in China roxadustat net revenues quarter-on-quarter.

China is the largest -- next slide, China is the largest dialysis market in the world. And there is an estimated 120 million people in China living with chronic kidney disease. In 2017, there was an estimated 600,000 patients in China on dialysis, but this patient population continues to grow rapidly. In addition, there are an estimated 1, up to 2 million dialysis stage patients who are not yet receiving dialysis treatment. We have seen meaningful adoption of roxadustat across a wide variety of patients segments and settings, including incident dialysis, stable dialysis, home dialysis, peritoneal dialysis and non-dialysis-dependent patients. This broad utilization is important because it informs us as to the different ways for roxadustat to potentially grow. The launch in China is going well, and we believe it has positive implications and read-through for the rest of the world. It gives us a lot of confidence for the role of roxadustat in both the non-dialysis-dependent and the dialysis-dependent patient populations.

Coming back to pamrevlumab. We are implementing a comprehensive plan to accelerate development across the 3 indications of idiopathic pulmonary fibrosis, locally advanced and resectable pancreatic cancer and Duchenne muscular dystrophy, once the situation with COVID-19 improves. Pivotal studies in all 3 indications will be enrolling this year, and we intend to give a more fulsome update on clinical trial status and time lines in the second half of this year. We also recently announced that we are planning clinical trials of pamrevlumab in the treatment of COVID-19. Given our expertise in CTGF biology and its potential application in lung disease, we have a unique approach with pamrevlumab in the treatment of patients suffering from severe pulmonary sequelae of the virus -- of coronavirus. These trials will determine if pamrevlumab treatment of hospitalized COVID-19 patients improves patient outcomes, both during the acute phase of infection and longer term.

Finally, these are upcoming -- these are the upcoming milestones for the remainder of the year. We look forward to publishing additional roxadustat data from our Phase III studies, including post analysis, and are expecting roxadustat approval in the U.S. by year-end.

Thank you very much for joining us for the meeting and for this brief presentation. Thank you.

Operator

Ladies and gentlemen, this does conclude the program, and you may all disconnect. Everyone, have a great day.

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FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

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Call Participants

EXECUTIVES

Enrique A. Conterno *CEO & Director*

ANALYSTS

Kyuwon ChoiGoldman Sachs Group Inc.,
Research Division

Presentation

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. Good afternoon, one. I'm Paul Choi, the SMid cap biotechnology analyst at Goldman Sachs. We'll continue with our next session here, which is FibroGen. And I'm very pleased to introduce from management, Enrique Conterno, who's, I think, a well-known quantity to investors. He's the CEO here at FibroGen.

I think as with other sessions, what we'll do is let Enrique do a few brief introductory remarks and give us an overview of what he's finding to be going on at FibroGen. And then we'll proceed with the Q&A. [Operator Instructions] And with that, Enrique, I'll turn it over to you for some opening comments.

Enrique A. Conterno

CEO & Director

Very good, Paul. Thank you very much for the invitation. It's a pleasure to be here.

I'm very excited with the agenda that we have at FibroGen. As I've mentioned in the past, we are very committed to 3 overarching goals. #1 is to ensure that regulatory and commercial success of roxadustat, and we are making excellent progress. I'm pleased with how the regulatory review is going. And also, I think it is important as -- when we look at the profile and some of our competitors starting to get some of the data basically reinforcing that we have a highly differentiated product profile in roxadustat, and we can speak a little more about that.

Second, overall objective is about accelerating the development of pamrevlumab. Of course we've been pursuing IPF. We are pursuing locally advanced and unresectable pancreatic cancer and finally we intend to start Phase 3 trial for Duchenne Muscular Dystrophy in the second half of this year. Three important indications that we have been discussing for quite some time. We had announced that we had paused the IPF studies, we paused that for a couple of months, but we have now restarted enrollment of the IPF studies. We paused it due to vulnerability of those patients to COVID-19 given their vulnerability when it comes to pulmonary function. And of course in DMD we are going to be starting, we believe, in the second half as I mentioned. Now in addition to those three important trials we announced yesterday that we are also starting trials in COVID and it is important just to give maybe a sense of how we are thinking about this. There are two main areas of COVID that we are studying. All of them in hospitalized patients. But one area is in the acute settings, where patients we believe that pamrevlumab can help with oxygenization so at the end patients should require less ventilators and basically really better survival over all. And then I think probably more evident than that is on the chronic side that we think about the patients that develop post being hospitalized and plus having COVID basically develop interstitial lung disease and they have fibrosis and we clearly given the data that we have from IPF, we view we have a very unique and important approach to try and ameliorate this fibrosis in those patients. So we clearly have a very interesting trial as well when it comes to that second setting. And finally the third overarching objective is to really reenergize our research agenda and bring new clinical candidates and bring new products. Really leveraging the scientific platforms that we have both around HIF biology and CTGF biology. So it is very exciting and we are planning to share more of that I think during an Analyst Day that we are planning to hold sometime in Q3 or Q4.

Question and Answer

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. Thanks for that overview, Enrique. Maybe we will start with the commercial piece because roxadustat is approved in certain international markets, specifically in China and Japan. Can you maybe give us a sense of what the commercial environment is like for you and your partner post-COVID and you know sort of what's happening in the China market- probably is most of interest to investors. And just has there been any inflection in recent weeks as China has been opening up?

Enrique A. Conterno

CEO & Director

Yes. I think as I've mentioned, we feel very good about our China launch. Just to recap, we had 5 million dollars of sales in net product sales of roxadustat in Q1. Keep in mind that Q1 has 2 months' worth of lock down in China, two out of three in the quarter. So in a certain way I think April was really the first month when we started to see basically China starting to return to a new normal. We have seen an important inflection on demand in China. Of course, I think we had talked about the listings and how much progress we are making on the listings. Which, at the end of Q1 we had shared that we were already accessing, based on hospital listings, over 30% of the overall market for CKD anemia in China both across DD and NDD. And those listings continue to improve, so what we shared in the Q1 earnings call was basically that we expect a meaningful ramp-up in revenue as we look at Q2 and beyond. So we are very excited and think I would qualify the launch as going very well.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. And by the way, I'm just getting some comments that maybe the audio and visual might be having a little bit of issues. So I do want the audience to know that we are working on it and hopefully Enrique's comments, which are more important than my questions are coming through. If something is not clear, please just let me know and I'll try to reiterate or summarize what Enrique is saying here. Then maybe just to follow up on the China side with regard to the NRDL, has that-how is that, in your view now that you are officially on the NRDL, change the market opportunity for you? It does effect the price in terms of downward pressure, but in terms of access, how does that change the dynamic for roxa there?

Enrique A. Conterno

CEO & Director

Well, as you know, I think NRDL's really for products in China -- really for the -- really, the launch of products in China that is really when you can have meaningful uptake for our products and when you can have meaningful listings. And we are very pleased with the price that we received. And at this point in time, it's -- the key objective for us is really to improve the number of hospitals where we're listed, and we are doing that at record pace. I'd like to compliment our partner, AstraZeneca, which is a force in China, in doing a terrific job. And we're seeing adoption in those hospitals. So we are basically seeing many of the pillars basically working.

One thing that is encouraging for me to look at China beyond the number of patients. So for us, is to look at the different types of patients that we're enrolling. It's not just generally DD and NDD. I had expected maybe the NDD uptake to be maybe slower, but we are seeing good uptake in NDD. And when it comes to dialysis, we're seeing home dialysis, we're seeing incident dialysis. We're seeing patients that were on prevalent dialysis. So it's -- we are seeing basically many different types of patients, which gives me a confidence that we have many ways of growing over time, which I think is very encouraging for us.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. And maybe the last question on China, and you touched on it. You're seeing mixed use in terms of the different populations as you indicated. Just in terms of how patients are responding to it and potential stickiness and adherence to therapy, I know it's early days, but could you maybe provide some color on this? Is this something that they're just maybe trialing for the near term? Or what is the adherence looking like, at least in the early days here?

Enrique A. Conterno

CEO & Director

I think it's a little bit too early to look at the adherence. But as you know, that is going to be key for roxadustat. Hopefully, a benefit that we can provide over other therapies, given its oral use and the overall efficacy safety profile, So that's something that is part of our agenda to ensure that patients are adhering so they can get a full benefit of the product. But it's a little bit too early to comment on what the adherence is.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. Great. Thanks. Understood. Maybe shifting gears then. You talked a little bit about competitor data here that's recently emerged. And you saw some competing data from another drug in the HIF category here. And we're also probably in a time frame where we could see some incremental updates in a different population. So I think you probably understand that we're talking about Akebia's data here. And so could you maybe provide your initial thoughts on what you saw with the dialysis population here? What does that mean perhaps from a competitive perspective for FibroGen here?

Enrique A. Conterno

CEO & Director

Yes. I think the data from the competitor validates the class, but it also reinforces the highly differentiated medicine that we have in roxadustat. And maybe I wanted to make a few comments on that. As I think about efficacy, which is so key, as you know we had with roxadustat, a statistical superiority on hemoglobin relative to EPO in DD. And when we look at the data of our competitor, yes, they were non-inferior clinically, but really -- relative to darbepoetin, but statistically inferior when you look at the results. Our hemoglobin mean was 10.86. Their hemoglobin mean was 10.36 -- sorry, 10.85 for us, 10.36 for them.

Now keep in mind and as you know, hemoglobin levels are related to transfusion. So the higher your hemoglobin in that 10 to 12 range, the lower risk of transfusion that you have. And we demonstrated a statistically significant reduction in transfusion relative to EPO.

It's also important to note that the cohort of patients on hemoglobin, 8 to 10 have about a three- to fivefold increase in the risk of transfusions relative to 10 to 12. And the standard deviation was a little bit above 1, I think, for the competitor product. For us, it was just slightly less than 1. So think about 10.36, standard deviation of 1, how many patients you have below 10. Think about our product, and therefore what is the real outcomes when it comes to efficacy.

Now in addition to that I think as you know, I've been very excited about our incident dialysis data and the fact that we showed a 30% reduction in MACE risk and 34% when it comes to MACE plus. Honestly, that's huge and that's an anchor. Because as patients start dialysis, clearly part of that dialysis initiation is going to be treatment of anemia. And I believe that we have the very best data. It's quite compelling and differentiated.

So I feel like we probably have the best of both worlds, validation of the class, but also a differentiated product.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Would your expectations for the upcoming competing data in non-dialysis-dependent population be any different here? Do you think the trial will succeed? Given your earlier comments on the class validation, is

there any reason to think it wouldn't work? Or are you looking primarily for differences on the periphery here as you highlighted with the dialysis population?

Enrique A. Conterno

CEO & Director

Yes. Let's wait for the data. Let's -- and I'll comment on the data once I see it, so I can comment, not speculate on it.

Kvuwon Choi

Goldman Sachs Group Inc., Research Division

Fair enough.

Enrique A. Conterno

CEO & Director

But I -- as you know, there's a difference in trial design in that we compare [ourself] to placebo, which I think gives us the very best chance to basically have a label without a black box, given that we showed basically comparable safety to placebo. It is very difficult to achieve that -- if the trial is designed with a comparator relative to a product that has a black box. Clearly that, from a regulatory perspective, really doesn't fly. So I also like our chances to get the very best possible label here.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. That's actually kind of related to an inbound question we received from an investor, if you don't mind. And just in terms of -- you talked about comparators. And is a placebo comparator, in your mind, a higher bar as you think about the regulatory process than comparing to EPO?

Enrique A. Conterno

CEO & Director

It is when it comes to safety, of course. And at the end, I think EPO have a black box, so ESAs has black box. So it is a much higher bar, right? So if you compare yourself to a black box, as you know we just released data from DOLOMITES yesterday. And as part of the data, we had a -- yes, very good efficacy, noninferior but as favorable on the efficacy side to darbepoetin, but the hazard ratio on CV was of course not a large number of events, but it was 0.81 for MACE and 0.9 for MACE plus. So I think it reinforces the profile. But regardless of what that result would be, if all of our trials were compared to ESAS, I think it will be extremely difficult to avoid a black box. So I do think it's a high hurdle. Keep in mind also that most patients in that setting are really not receiving an anemia treatment. One statistic that I've shared in the past is that when you look at the 12 months prior to initiating dialysis. So these are patients before going to the 12 months prior, only 14% of them are on a ESA treatment in the United States. That's a very low number. So I think what that tells me is there's a huge opportunity to increase the treatment rates, not just in the 12 months, but we're going to be looking at stages 3 to 5 and making sure that everybody is really receiving the proper standard of care and treating anemia when appropriate. And I think that's a very important opportunity for us. And quite frankly, I think we're offering a product now that is going to be -- has a safety profile that doe not exist in NDD. So I think the possibilities are very significant for us.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. So maybe sticking on the topic of data. You mentioned DOLOMITES. But maybe if we could go back a few months to ASN meeting last year, you presented some detailed data across your studies. But one of the questions, I think, that remains on the mind of investors is just given what you presented at ASN, what is your current thinking on a potential advisory committee meeting for roxa later this year? Especially it got a little trickier given the FDA is operating in a COVID environment. And just maybe do you expect a meeting? Is that going to happen? And just where are you in terms of preparation for that?

Enrique A. Conterno

CEO & Director

As we've shared in the past, we have received no indication from the FDA of an Adcom. Typically, sponsors -- the FDA shares with the sponsors that they should plan for an Adcom, either prior to submission or during filing acceptance. We are having our mid-cycle review later this month. That is, we can call it almost the last opportunity for the FDA to say, hey, we're going to plan. It will be very late, but it could be a time when the FDA could say we -- they want to look at that. Clearly, after that data I think the chance of an Adcom, I think, decreases exponentially. So I -- at this point in time, nothing has changed. We feel very good about our data. I think I remember the first time we met and I shared with you, I found the data very compelling on the CV side as well. On the CV safety side, one is comparable or relative to placebo and NDD when the alternative today basically has a black box. So that's a great scenario. And relative to EPO in DD, in incident dialysis where there are so many risks for CV events, we basically have a 30% reduction in MACE. That's an unbelievable result. So I find the data very compelling, and I don't believe the CV data -- safety data warrants a black box.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. Thanks for that, Enrique. Maybe digging into the data a little deeper that you presented. In terms of the MACE end point that you referenced, in all 3 populations, it was below the historical 1.3 standard that's typically been used in this sort of population. But some of the individual components were above that. And can you -- you said your mid-cycle review meeting is coming up here. But I guess, what's your -- the company's perspective on when thinking about the composite end point and how the agency might view that, versus some of the individual components that did show somewhat higher upper bounds with regard to the confidence intervals?

Enrique A. Conterno

CEO & Director

Well, the higher bounds for the subcomponents, including some that are below 1, the ones that are below 1 is because you have a smaller sample size. That's just a function of the sample size. Clearly, you design the trial and the sample size to be able to meet a certain -- to be able to rule out a certain level of excess risk, okay, in this case I think 1.3 or 30% excess risk.

Typically, what the FDA will look at is they will look at MACE, and they will basically look at the entire pool, which is for DD and for NDD and look at the benefit/risk profile of the product. I feel like -- I feel that we have with roxadustat, we have a very favorable benefit/risk profile.

When it comes to the sub-endpoints, when it comes to whether it's death or MI or stroke, I -- what FDA is looking at is whether any of those sub-endpoints basically are statistically significant when it comes to harm. So -- but in all of the cases for our studies and the pooled analysis for both DD and NDD, the confidence interval actually includes 1. So we don't have that issue. But that could be, even though the study is not powered to do that, that could be a question that the FDA has if you have one of the subcomponents to basically have the entire confidence interval to the right of 1, if you wish. That's not our case.

So in a certain way when I look at the interim data, I think as I look at principles as I've -- as you know, I had a chance to run CV studies in my previous roles. I basically feel like we meet a number of different filters that make me feel very confident about the strength of the data from a commercial safety and a regulatory perspective.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. That makes sense. Maybe just to talk a little bit about one of the populations that that gets a little bit overlooked relative to dialysis or non-dialysis, that's the incident dialysis population. And as a reminder for investors, this is a population that has had basically minimal exposure historically to EPO or very limited exposure. And in terms of the trial, this is the one subgroup or the one population that didn't show an improvement on MACE here. Is this also, Enrique, an artifact of the trial sizing and design? And maybe

more from a commercial perspective and regulatory perspective, how are you approaching the opportunity in this particular population?

Enrique A. Conterno

CEO & Director

Yes. So as you said, I think we showed a significant benefit when it comes to MACE in this population, 30% reduction in MACE. Just for your audience, incident dialysis is basically we enroll patients that basically were starting dialysis, the definition is within the first months of starting dialysis to be enrolled in this particular trial. And we had 1,500 patients in this trial, so a fair amount of patients. And what we -- as you know, these patients are at significant risk because of the transition. It is one of the riskier times for patients. And I think the results are quite compelling. Unfortunately, as you know survival with dialysis is not good. So patients after 5 years don't have a great chance of survival in some cases. So giving them the best chance by whenever they start dialysis to have -- to basically be on a treatment that has such compelling MACE results, I think is incredibly important. So I feel it is the natural point when the treatment decision for anemia will be made starting dialysis and where we have probably the most compelling data that we have.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay, interesting, right. Maybe continuing on the commercial front here, Enrique. In terms of the U.S. market, it's -- in terms of dialysis providers, it's essentially a duopoly dominated by 2 companies, specifically DaVita and Fresenius. Can you maybe comment on what's been happening with regard to your discussions with these potential providers? What is the feedback been on the roxa data, and perhaps how are they thinking about implementing or integrating roxa into their treatment paradigms there?

Enrique A. Conterno

CEO & Director

Clearly, as you can imagine first, we have close relationships with dialysis organizations, the 2 large ones you mentioned and others as well. Clearly, we've been working with them because we run our clinical trials and they were part of that. And clearly we are in discussions, thinking about how to ensure once we get approval, that we can have the most success incorporating roxadustat into different protocols. Clearly, that's a decision that each one of those dialysis organization will have to make.

A pretty important part of that decision-making process is reimbursement. And as you know, we have a framework from CMS called TDAPA, which is basically the add-on payments for products that bring innovation and that in order to basically create an incentive for dialysis organizations to include these products into their protocols, given that they have a bundle that is capitated, they are going to be providing this add-on payment. This add-on payment is 100% of the ASP, or average selling price, and we believe that roxadustat is eligible. The process for this to happen is you once you get approval, you apply for this, then you would basically get authorized for -- to be included in TDAPA. We believe that roxadustat is eligible, and we intend to apply for it.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. So just to remind audience who may be listening here, this TDAPA technology innovation premium that you referenced would be incremental to the fixed bundle that these centers currently get for treatment and for drug. That's correct?

Enrique A. Conterno

CEO & Director

That is correct.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. Great. So one of the things, I guess, in terms of your last steps here is as you think about commercialization here and the footprint in the U.S. is thinking about the competitive landscape and ultimately perhaps pricing. You've obviously mentioned that you're talking about your discussions with some of the larger dialysis providers here. But how does pricing in the U.S. perhaps potentially look like in your mind relative to what it's been established in terms of your existing commercial markets like China and Japan? And then how do you think potentially about what the commercial landscape might look like in Europe where your partners are also seeking approval for roxa?

Enrique A. Conterno

CEO & Director

Yes. It's an excellent question. Clearly, we want to make sure that we are pricing our products relative to the value, a significant value that the product can provide. We won't be discussing specific pricing strategy as you can imagine, until basically we launch the product, we don't think that will be in our best interest to disclose that now. But we need to ensure when we look at the U.S., that we are looking at all the benefits that the product basically provides and from a clinical and from an economic perspective to the system. And then making sure that we are pricing the product appropriately to what it offers. Clearly, when it comes to different settings or different markets in Europe for example, Europe in many markets -- most markets in Europe, they tend to anchor to a specific price. Which is why in Europe, you typically need a trial like DOLOMITES, for example, that allows you to basically bridge from the anchor price, maybe from an ESA and how do you bridge that to a price for in this particular case for roxadustat. So you still do the formal economic analysis, but the process is a little more rigid, I think, than in the U.S.

I'm excited about, honestly how transformational this product could be when it comes to the treatment of anemia, first in CKD of course. But keep in mind that we're also pursuing other indications, 2 that we have shared in chemo-induced anemia and also MDS. So very exciting opportunity for us to really revolutionize the treatment of anemia.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Sure. That actually provides a nice segue to talk about these additional opportunities for roxa. Obviously, investor focus has largely been in the past year or so on regulatory landscape. But you are also running an ongoing Phase III in MDS, and you've published some very interesting data there. Can you maybe talk about what is the next potential update for the MDS study? What is the enrollment status right now?

And then in terms of the competitive landscape, there's a drug approved out there for treating anemia for MDS related patients. Can you maybe just think about how clinicians might view roxa in this population, given that there is an approved therapy out there for patients with anemia who have MDS?

Enrique A. Conterno

CEO & Director

Yes. Clearly, it's -- as you know, this is a highly vulnerable population, and we are delighted with the progress that we're making. I think through the COVID-19 epidemic, I think we've continued to see good progress in the enrollment of our Phase III study in MDS. There is indeed a therapy approved, but keep in mind that this is -- they have a much narrower label. It's really for ring positive and really as a second line to patients that have failed on ESAs. And our study really looks at both ring positive and negative and whether they are naive to ESAs or failed on ESAs. So we probably have a population segment that is probably 3x as large as the current approved therapy. So we're excited about that trial and what -- looking at our results, we should be able to see something on that trial sometime next year.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Next year on that. Great. And then you also referenced what could also potentially be a very broad population as well, which is chemotherapy-induced anemias. I think that's also something like MDS that gets overlooked a little bit there. Can you maybe give us an update on what are your plans there? You

obviously have your plate full with roxa in dialysis and your regulatory situation, but you have the Phase III going on in MDS. What's the plan to sort of expand the opportunity set here with CIA?

Enrique A. Conterno

CEO & Director

So CIA as you know, we're in Phase II. We'd like to conclude as soon as possible and then enter Phase III. Keep in mind that we have around 1.3 million patients with chemo in the U.S. And depending on the area, you could be looking at rates of anemia between 30% and 90%. So there is a very significant need when it comes to chemo. So we are trying to make as much product as we can as fast as we can because we think that this opportunity is very meaningful.

Keep in mind that ESAs used to sell almost \$4 billion in this segment back in the mid-2000s. So they had a very significant use in this setting. And when you look at blood transfusions in the United States, about 15% of the blood transfusion are in heme-oncology, so hematology-oncology. That's -- it's -- there's a very significant need, and I believe that we can also play an important role.

Kvuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. Thanks for that. So maybe sticking with the pipeline here and switching gears to pamrevlumab. I think the program that you talked about earlier in IPF, it was on pause. And you talked about it resuming here, but you're also planning a second trial. So I was wondering, can you maybe comment on when that second trial might potentially kick off here? And just what are sort of -- what does enrollment look like for the first trial now that you resumed that? And then maybe we can talk about the commercial opportunity after that as well.

Enrique A. Conterno

CEO & Director

Yes. So one of the reasons we're excited about pamrevlumab is because when we look at the Phase II results, which were published in the Lancet, we see an effect size on forced vital capacity that is basically larger than products that are today standard of care or any product that I can see in development. So we have once again a very differentiated product on the efficacy side and it's highly tolerable.

In addition to that, it is really the only product that in IPF that when you look at imaging, you basically can see reversal of fibrosis. So it's a very exciting profile. Keep in mind that the Phase III trial was designed in such a way that it is very close to the Phase II, which I think always increases the likelihood of success.

We're going to be providing a full update on the time lines for this trial and others on pamrevlumab during our Analyst Day in Q3 or Q4. So we look forward to that. I think what I would say is clearly when you look at enrollment, one of the most important things for enrollment is site activation. We are making great progress in site activation. One of the things we've done is geographic expansion of where we are enrolling patients. So in Asia whether it's Korea or Taiwan or in Europe, but also we intend to start enrolling patients in China likely in Q3 of this year. So we -- with that geographic expansion, it allows us to activate many more sites and really accelerate the enrollment in a really big way. So I'm excited about our plans to bring the therapy to patients as soon as possible.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Great. And you talked a little bit about the patient population here. And so I think you were probably referring to Esbriet, which is the approved therapy in the indication. But can you maybe remind us, are the trials designed to be a second-line therapy? Is this supposed to be something that would displace it in the front line? How do you think about the target population ultimately for pamrev here in IPF?

Enrique A. Conterno

CEO & Director

Yes. In ZEPHYRUS 1, we are enrolling patients that are naive to therapy and patients that have failed the standard of care. As you know, only less than half of the patients really are able to be on the standard of care for a number of different reasons, including tolerability reasons. So the idea with this product is to truly -- if we can show results not only when it comes to forced vital capacity where we can have the largest effect size of any product when it comes to pulmonary function, but if we can also look at some measures when it comes to disease progression and the fact that we can have a significant impact there, I think this product could be pretty transformational. And I believe that the product, yes, in some cases, is going to be used with other products or -- but in many cases, why not utilize this product as your firstline product? It's all going to depend on at the end, on the Phase III trials. But if they replicate -- if we replicate what we saw in Phase II, I think our chance to become standard of care, first line, are very significant.

Kyuwon Choi

Goldman Sachs Group Inc., Research Division

Okay. We're pushing our timing here. But Enrique, I want to maybe spend a little bit of time talking about strategy here and particularly with regard to the third leg or aspect of the story. You talked about particularly with regard to investing in discovery and research here. And just -- you have you a pretty full plate right now with roxa in 3 indications and then developing pamrevlumab for 3 indications. But just at what point do you think about reinvesting in the business, emphasizing discovery again and just maybe potentially adding a third leg to the story here?

Enrique A. Conterno

CEO & Director

Yes. We are really putting a lot of focus on that area. Of course, that today is not visible to investors, but I find very significant opportunities to basically develop -- to think about HIF biology and develop new compounds. They're not necessarily going to be HIF-PHIs, okay? So I think there are many opportunities for us. But if you look at whether it's preclinical models or you just look at the underlying biology of the HIF class, it is pretty clear that you could be impacting many different diseases or disorders. And it's very exciting for us to think about that. I would disclose some more during our Analyst Day, probably not enough to -- for you to say, wow, exactly, tell me more, but enough to maybe whet your appetite of how exciting this area is and all the different opportunities or the reasons to believe.

And I think similarly for CTGF biology, of course we have pamrevlumab. We could think about what additional indications we could pursue with that asset. But also we need to be thinking about how do we leverage CTGF biology to develop new clinical compounds and being able to bring the next leg of this -our innovation story to patients. So I'm very excited about that. I think it's very promising.

Kvuwon Choi

Goldman Sachs Group Inc., Research Division

Great. It sounds like the Analyst Day or R&D Day coming up here will be really interesting for multiple reasons. Unfortunately, we've come up here on our time limit. Enrique, thank you so much for participating again in the GS conference, and we'll see you again soon.

Enrique A. Conterno

CEO & Director

Thank you very much, Paul.

Kvuwon Choi

Goldman Sachs Group Inc., Research Division Okay, thank you.

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FibroGen, Inc. NasdaqGS:FGEN FQ2 2020 Earnings Call Transcripts

Thursday, August 06, 2020 9:00 PM GMT

S&P Global Market Intelligence Estimates

		-FQ2 2020-		-FQ3 2020-	-FY 2020-	-FY 2021-
	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS	CONSENSUS	CONSENSUS
EPS Normalized	(0.79)	(0.95)	NM	(0.67)	(2.33)	(0.88)
Revenue (mm)	48.29	42.89	V (11.18 %)	52.57	263.69	438.02

Currency: USD

Consensus as of Jul-28-2020 5:30 AM GMT

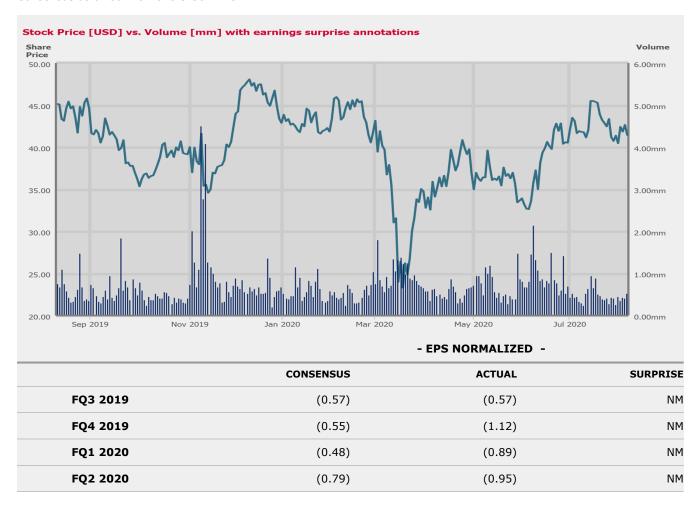


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Michael Tung Investor Relations Executive

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Michael Jonathan Yee Jefferies LLC, Research Division

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Presentation

Michael Tung

Investor Relations Executive

Thank you, Ashley, and good afternoon, everyone. I'm Michael Tung, Vice President of Corporate Strategy and Investor Relations at FibroGen. Joining me on today's call are Enrique Conterno, our Chief Executive Officer; Thane Wettig, our Chief Commercial Officer; Pat Cotroneo, our Chief Financial Officer; Dr. Peony Yu, our Chief Medical Officer; Chris Chung, our Senior Vice President of China Operations; and Dr. Elias Kouchakji, our Senior Vice President of Clinical Development, Drug Safety and Pharmacovigilance. The format for today's call includes prepared remarks from Enrique and Pat. After which, we will open up the call for Q&A.

I would like to remind you that remarks made on today's call include forward-looking statements about FibroGen. Such statements may include, but are not limited to, our collaborations with AstraZeneca and Astellas; financial guidance; the initiation, enrollment, design, conduct and results of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities; commercial results and results of operations; risks related to our business; and certain other business matters. Each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those projected in that statement. For a more complete description of these and other material risks can be found in FibroGen's filings with the SEC, including its most recent Form 10-K and Form 10-Q. FibroGen does not undertake any obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise. The press release reporting our financial results and business update and a webcast of today's conference call can be found on the Investors section of FibroGen's website at www.fibrogen.com.

And with that, I would like to turn the call over to Enrique Conterno, our CEO. Enrique?

Enrique A. Conterno

CEO & Director

Thank you, Mike. Good afternoon, everyone, and welcome to our second quarter 2020 earnings call. Despite the challenges presented by the COVID-19 pandemic, on behalf of FibroGen, I'd like to reassure patients, health care providers, investigators and stakeholders of our continued commitment to bring our potential first-in-class medicines to patients suffering from chronic and life-threatening conditions. We continue to monitor the situation closely. To our employees and our patients and to the health care providers, regulators and countless others who interact with FibroGen, please know our thoughts are you and your families.

I want take a moment to welcome both Dr. Aoife Brennan and Dr. Ben Cravatt to our Board of Directors at this exciting point in Fibrogen's history. Aoife's experience in rare diseases and clinical development and Ben's world-class expertise in biology and chemistry will provide invaluable perspective to our Board.

With today's earnings call, we are implementing a new format with a goal to improving communications with the investment community and other stakeholders. I will begin by providing a high-level summary of the most important accomplishments and developments from the second quarter. Pat Cotroneo, our CFO, will then review the financials. After which, we will open up the call to your questions. Today's updates will include our China results, U.S. regulatory review and our clinical trials. We hope this new format will result in more time for us to have a constructive dialogue.

So let us get started with our strong China results. With a return to a new normal business environment in China, we are pleased to report net sales of roxadustat of \$15.7 million for the second quarter. This represents an increase from the \$5 million in China net sales reported the first quarter. We are most encouraged by the trajectory of the launch, which is being driven by both an expansion in hospital listings and continued adoption. Hospital listings continue to be a key focus of our launch efforts. Notably, as of the end of the second quarter, roxadustat was listed as hospitals representing over 45% of the CKD anemia market opportunity in China. This is in comparison to the over 30% reported at the end of the

first quarter. We're especially pleased with the penetration at top-tier Class IIIA institutions, which are generally the larger ones and the hospitals were key opinion leaders and early adopters practice.

We continue to see broad roxadustat utilization across different patient populations, including in the hemodialysis, peritoneal dialysis and non-dialysis populations. Utilization across these different patient populations bodes well for long-term success and provides important learnings as we prepare to launch roxadustat in the U.S. and other countries.

Finally, we recently amended our China collaboration with AstraZeneca. The new agreement more optimally aligns both FibroGen and AstraZeneca to maximize the economic value of the roxadustat franchise and will result in improved and more predictable economics and profitability for FibroGen. We look forward to keeping you updated as we advanced our long-term goal of making roxadustat the standard of care in treating China's CKD anemia patients.

Let us turn now to the U.S. regulatory review and commercial preparation for roxadustat. We had our mid-cycle review with the FDA in June and continue to expect an FDA decision on the roxadustat NDA by the PDUFA date of December 20, 2020. The FDA has indicated that an advisory committee meeting is not planned at this time. Overall, we are pleased with the cadence of an engagement with the FDA. While future interaction with the FDA are planned, given the proximity of label discussions, we will no longer be commenting on those interactions until the PDUFA date. On the commercial front, we appointed Thane Wettig to the newly created position of Chief Commercial Officer, where he will lead FibroGen's commercialization efforts. Thane brings more than 30 years of global biopharmaceutical leadership and experience, and we welcome his leadership in this area. Thane is working closely with our partners, AstraZeneca and Astellas, to ensure roxadustat will reach as many CKD anemia patients as possible on a worldwide basis.

We continue to work closely with AstraZeneca regarding U.S. launch preparation activities. Within the next few months, we expect to have submitted up to 10 manuscripts covering the Phase III data, both individual trial and pooled data sets. At the upcoming American Society of Nephrology Congress in October, we expect to present a meaningful number of abstracts on roxadustat and HIF-PHI science. We continue to engage with CMS on the Transitional Drug Add-on Payment Adjustment, or TDAPA. Finally, disease awareness activities imperative to reframing the primary defect of CKD anemia from one of EPO and iron deficiency to an oxygen-sensing deficit are under way in the U.S.

In Europe, the filing for roxadustat for the treatment of anemia in adult patients with chronic kidney disease was accepted by the European Medicines Agency in May. Our partner, Astellas, expects a European approval decision mid-2021.

Moving now to our pipeline, starting with newly initiated clinical trials. In June, we initiated 2 separate trials studying pamrevlumab in patients hospitalized with COVID-19. In the U.S., we initiated a Phase II study investigating the efficacy and safety of pamrevlumab in hospitalized patients with acute coronavirus infection. This multicenter trial will enroll approximately 130 patients with COVID-19 and will assess patient time to and on ventilatory support.

In Italy, a Phase II/III investigator-initiated trial investigating the efficacy and safety of pamrevlumab in approximately 68 patients hospitalized with COVID-19 was started. The primary objective of this study is to assess the effect of pamrevlumab on blood oxygenation in patients with COVID-19 infection in the acute and post-acute settings. The majority of patients suffering from severe forms of COVID-19 have bilateral interstitial pneumonia-causing reduction in oxygenation and severe respiratory failure. The administration of our anti-CTGF antibody, pamrevlumab, could protect the lung from the immediate consequences of the infection presented as acute respiratory distress syndrome.

Now moving to an update of our ongoing clinical trials. The COVID-19 pandemic continues to present challenges to the conduct of clinical trials across our industry. The most effective of our trial continues to be pamrevlumab's ZEPHYRUS IPF trial in which we temporarily paused enrollment for 2 months due to the vulnerability of this patient with severely compromised lung function. We have reopened ZEPHYRUS for enrollment and the remainders of our studies in locally advanced and resectable pancreatic cancer, myelodysplastic syndrome and chemotherapy-induced anemia continue enrollment, albeit at slower rates.

We expect to initiate LELANTOS, a Phase III trial of pamrevlumab in patients with non-ambulatory Duchenne muscular dystrophy this quarter, and we plan to publish updated 2-year data from a recently completed Phase II DMD study before year-end. We remain focused on accelerating enrollment of all of our ongoing clinical trials while ensuring patient safety.

I will now turn the call over to Pat Cotroneo, our CFO, to review the financials. Pat?

Pat Cotroneo

Chief Financial Officer

Thank you, Enrique. As announced today, total revenue for the second quarter of 2020 was \$42.9 million as compared to \$191.6 million for the second quarter of 2019. The current quarter revenue consists of net product revenues of \$15.7 million for roxadustat sales in China, \$19 million in development revenue and \$8.2 million of API sales in Japan. For the same period, operating costs and expenses were \$128 million and net loss was \$85.3 million or \$0.95 per basic and diluted share as compared to operating costs and expenses of \$78.7 million and a net income of \$116 million or \$1.34 per basic and \$1.26 per diluted share for the second quarter last year. Included in operating costs and expenses for the quarter ended June 30, 2020, was an aggregate noncash portion totaling \$23.6 million, of which \$17.6 million was a result of stock-based compensation expense as compared to an aggregate noncash portion of \$21.9 million, of which \$17.6 million was a result of stock-based compensation expense for the same period in the prior year.

At June 30, FibroGen had \$716 million in cash, cash equivalents, restricted time deposits, investments and receivables. During the second quarter of 2020, we received \$50 million for a milestone payment from AstraZeneca relating to the FDA's acceptance of our U.S. NDA filing and \$130 million of milestone payments from Astellas in connection with the EU MAA filing. Both of these milestones were recognized as revenue in the prior year when achievement became probable. Based on these milestone payments and our latest forecast data, we continue to estimate our 2020 ending balance of cash, cash equivalents, restricted time deposits, investments and receivables to be in the range of \$720 million to \$730 million, assuming U.S. NDA approval in Q4 2020.

Looking ahead, we have a total of \$245 million in anticipated milestones expected over the next 12 months for anticipated U.S. and EU approvals and first commercial sale in the U.S. At this point in time, we have no changes in our expectations in any of the anticipated milestones over the next 12 months. Thank you.

And I would now like to turn the call back over to Enrique.

Enrique A. Conterno

CEO & Director

Very good. Thank you, Pat. And in summary, FibroGen is well positioned. Our business continuity plans are in effect. And while we're seeing some impact to our operations resulting from COVID-19, we have the capabilities and resources to navigate through these uncertain times and achieve our stated goals. As roxadustat sales ramp up in China, our financial position is strong with approximately \$716 million in cash at the end of the second quarter. The EMA's acceptance of the roxadustat filing for treatment of anemia in adult patients with CKD triggered milestone payments of \$130 million from Astellas to FibroGen. In addition, we have a total of \$245 million in anticipated approval and first commercial sale milestones expected over the next 12 months. We received full partner reimbursement for all developments and commercialization of roxadustat in all geographies, except China, where we shared these expenses 50-50 with AstraZeneca. Based on our current forecasts, we are reiterating our estimated 2020 ending cash to be in the range of \$720 million to \$730 million, and we're well financed for years to come. Ashley, if you could now open the lines for questions.

Question and Answer

Operator

[Operator Instructions] Your first question comes from Geoffrey Porges with SVB Leerink.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Congratulations on the positive regulatory interaction. I have to ask a little bit about that. So perhaps, Enrique, you could give us a sense of how important to the commercial opportunity is whether or not you get a black box warning for CV risk. And then secondly, could you give us a little bit more color how the China agreement with AstraZeneca has changed? And particularly how it may have influenced your flexibility with respect to the ownership and integration of that business unit?

Enrique A. Conterno

CEO & Director

Very good, Geoff. Thank you for your questions. Let me try to answer first your -- the second part of your question related to the update in our China agreement with AstraZeneca. Clearly, we believe that this updated agreement best aligns I think both organizations to maximize the economic value of roxadustat. Importantly, this agreement allows us to have both more predictable but also improved economics for FibroGen. So we are excited about having been able to update this agreement and given the significant opportunity that we see with roxadustat that has a very good chance of becoming a blockbuster product in China. I think you were referring how this impacts other future plans. I think it's -- as I mentioned in the past, we're not prepared to comment on that. But I think, if anything, having this agreement I think gives us more flexibility to do anything because I think we have a great foundation for our business in roxadustat.

As it relates to a boxed warning, as I mentioned, we're not planning to make comments when it comes to labeling going forward. But clearly, we view that roxadustat will be successful -- I think I've mentioned this to you and others in the past, very successful regardless. Clearly, we need to look at the entire label. And when we look at the label for roxadustat, including a potential boxed warning, it's going to be what does the labor in totality says and our ability to fully commercialize roxadustat, given all the benefit that it can provide. We continue to view that our data shows a very positive benefit-risk profile for the product.

Operator

Your next question comes from Michael Yee with Jefferies.

Michael Jonathan Yee

Jefferies LLC, Research Division

Congrats on the progress. Two questions for me. Enrique, I know you can't comment specifically on FDA discussions. So I guess my question is more about what sort of the key takeaways are from your mid-cycle review meeting? And what are the key shall I say, gating steps for you as you get to the end of the year on the review? Second question is on China. Maybe you can make a comment or Chris could make a comment. Obviously, a pretty strong number in the second quarter. Maybe you could just shed a little more light on that. Is there anything particularly surprising that could be a read-through to the United States, et cetera, et cetera? The United States has a different reimbursement model, of course. So maybe you could talk to how much can we read-through into things.

Enrique A. Conterno

CEO & Director

Very good. Thank you, Michael. Basically on the mid-cycle review, I think, clearly, it is -- the mid-cycle review is an overall update of our submission. But when it comes to news, as we've shared, the FDA indicated to us that there's no outcome that is planned at this stage. Clearly, you are asking about other

types of interaction with the FDA going forward. I think it should be no surprise, but clearly, labeling discussions are critical, and those will be starting soon. And of course, we need preapproval inspections and so forth. But our engagement and our interaction with the FDA was positive. So we feel good about the progress that we are making. As it relates to China, I'm going to allow Chris to give us a little more detail and color on our strong results there. Chris?

Christine L. Chung

Senior Vice President of China Operations

Thank you, Enrique. Michael, so obviously, we're very pleased with the results of the second quarter. It's a big jump from Q1. That is primarily due to increases in 2 things: hospital listings and market adoption. We looked at our channel sales. There's nothing spectacular about it. We believe it's very consistent with the market. So in terms of reading through to the future of China and the U.S., I think it just tells you the strength of the roxadustat as a drug that delivers significant benefits and efficacy to multiple patient populations, profile. And in particular, in peritoneal dialysis and non-dialysis, the oral convenience is a very attractive feature over ESA.

Enrique A. Conterno

CEO & Director

Yes. I think...

Michael Jonathan Yee

Jefferies LLC, Research Division

So to be clear, do you see good adoption in non-dialysis? I guess that was the sort of the real word of the question, too.

Christine L. Chung

Senior Vice President of China Operations

We have been very encouraged by the adoption in non-dialysis. We had anticipated that the launch market would be in dialysis, but the non-dialysis adoption has pleased us in a very positive way.

Enrique A. Conterno

CEO & Director

Yes. I think, Michael, clearly, I think what you're sensing from us is quite a bit of optimism. I think probably you sensed it during the last earnings call, but now we have some good sales results to show the progress that we're making. We are very pleased with the adoption of roxadustat in different patient populations. And you spoke about what are the implications for this to other countries? Of course, different countries have, including the U.S., different reimbursement schemes and -- but when it comes to physician adoption, I think we see a lot of read-through in terms of the benefits the health care professionals are seeing with roxadustat.

Operator

Your next question comes from Annabel Samimy with Stifel.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

This is Edwin on for Annabel. First maybe to follow Mike's question on China. We learned that in the first half, there are about 40,000 patients treated with roxa. How many of them are DD or NDD patient, if you could split them up? And how many new patients added in the second quarter? What is the launch curve do you project in the coming quarters? And then I have a follow-up, if I may.

Enrique A. Conterno

CEO & Director

Yes. I'm going to ask Chris to answer that question in China. As you know, we don't provide forward-looking forecast when it comes to roxadustat at this time. But maybe, Chris, you can provide some additional color around China.

Christine L. Chung

Senior Vice President of China Operations

Absolutely. Edwin, at this point in time, in terms of these segments, we believe 2/3 of the patients currently using roxadustat are dialysis patients, which is hemodialysis and peritoneal dialysis with the other 1/3, which is a very strong 1/3, being from non-dialysis. At this point in time, the 40,000 number is an estimate based on sales and assumptions about pricing, compliance and DOT. The increase has been from about 15,000 at the end of the first quarter to 40,000 now. It's a very nice trajectory. Obviously, looking into the second half of 2020, there will be changes in duration of treatment because many hospitals are just getting listed and reimbursement has just been implemented by the end of Q1. So at this point in time, it will be very difficult for us to project, but we continue to be very optimistic about the upward trajectory we're seeing in China.

Xiaodong Zhang

Stifel, Nicolaus & Company, Incorporated, Research Division

Great. And 2 regulatory questions. Do you think the chance for possible Adcom is significantly reduced at this point? And secondly, on CMS negotiation, have you got any preliminary agreement with CMS on the bundling issue? When do we expect any clarity on the progress with CMS, before or after roxa approval?

Enrique A. Conterno

CEO & Director

Very good. Let me try to provide maybe a reinforcement on the question related to the Adcom. So clearly, with the indication of the FDA that no Adcom is planned at this time, I think the likelihood of having an Adcom has decreased significantly. It doesn't mean that an Adcom could not be called or it's -- but it is -- the FDA is not planning for one at this stage based on the engagement that we had with them at the midcycle review.

In terms of CMS discussions, clearly, we have those discussions, but there's no such a thing as an agreement other than we will have to submit. Once we get approval, we will have to submit to CMS for the inclusion on TDAPA. And that can be done as soon as we get approval and then FDA -- the CMS will basically process that as quickly as possible. And we are -- we've done all the homework to ensure that we are ready and that we are hopeful that we can get expedited approval. I'm going to ask maybe Thane Wettig, our chief -- our newly appointed Chief Commercial Officer, maybe to make some additional comments. Thane?

Thane Wettig

Chief Commercial Officer

Yes. Thanks, Enrique. I think just to add to what Enrique said, the most important date for us is approval. And once we get approval, AstraZeneca and FibroGen will file for a HCPCS code, and then that starts the TDAPA review process. Now CMS' goal with TDAPA is to make the product available as quickly to their beneficiaries as they possibly can. And they state in their regs that their goal is to make TDAPA available within 90 -- or within the quarter within 90 days. And so that's the expectation that we have. And rest assured that we and AstraZeneca are doing everything in our power to assure the earliest possible availability of TDAPA for roxadustat.

Operator

Your next question comes from Joel Beatty with Citi.

Joel Lawrence Beatty

Citigroup Inc., Research Division

I guess, following up to the last question on TDAPA and the 90-day window, can you help provide some context of that kind of the gate-limiting factor to launching in dialysis centers? Or are there other things that need to take place, such as negotiations with the dialysis centers in order to start selling product there?

Enrique A. Conterno

CEO & Director

Yes. I'm going to -- great question. I'm going to have Thane comment, but you really need both, right? You really need TDAPA, and you really need to have the discussion with the dialysis organizations.

Thane Wettig

Chief Commercial Officer

Yes, that's exactly right. And in addition, for the dialysis-dependent patient population, our estimate is that about 2/3 of those patients will -- are currently being treated through the ESRD Prospective Payment System. And so there's about 1/3 of the patients that also go through Medicare Advantage as well as commercial. And so we'll be working actively with the priority payers. Between now and not just when product is available, but between now and even launched, having those conversations to set the stage for availability of roxadustat not only through the TDAPA designation but also through the private sector as well.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. And then maybe just one follow-up to that. How important are agreements such as the one that Akebia has with Vifor to the dialysis market? Is that something that would be an impediment to your launch? Or is that the type of agreement that you may be exploring as well?

Enrique A. Conterno

CEO & Director

No. We -- honestly, we do not view that we have a restriction or any type of limitation for us to be able to have agreement with any of the dialysis organizations. So at this point in time, we feel we're in a very good position.

Operator

Your next question comes from Jason Gerberry with Bank of America.

Jason Matthew Gerberry

BofA Merrill Lynch, Research Division

Enrique, just to follow-up on that last comment. What do you think the value is of having a contractual arrangement with the dialysis organization for a company like Akebia if you don't view it as an impediment to your ability to garner uptake in the market? And then my other question is, can you talk a little bit about how you see the China hospital listing progressing in the second half? Just kind of curious how you're seeing that progression going versus the benefit we saw in 1Q from 2Q.

Enrique A. Conterno

CEO & Director

Yes. I think on -- thank you for your question. I think on the first question is really -- I'm not sure this is a question for FibroGen. It's probably a question for Akebia, given they're the one that pursued that agreement. When it comes to hospital listings, as we mentioned, we went from basically over 30% to over 45%. So we were at over 30% at the end of Q1. We are now over 45% at the end of Q2. If we were to benchmark some of the blockbuster products in China, innovative blockbuster products in China, I think you will see that this level of penetration and when it comes to the overall opportunity in China to be at 45% of that opportunity, I think, is very significant milestone and achievement, basically at the second

quarter post-launch. So we feel extremely good. We expect to continue to make progress, but we do not provide formal forecast whether it comes to either revenue or listing for future quarters at this stage.

Operator

Your next question comes from Difei Yang with Mizuho Securities.

Difei Yang

Mizuho Securities USA LLC, Research Division

Just a couple. The first one on roxa in China. I know it's in the early days, but for dialysis patient population, do you see most of the prescriptions going to ESA failure patients or do you see adoptions across the board in that population?

Enrique A. Conterno

CEO & Director

Yes. Let me once again call on Chris to give us some additional color on some of these dialysis-dependent patients. Are they ESA failures or treatment naive or what can you tell us?

Christine L. Chung

Senior Vice President of China Operations

So we are seeing adoption across all those patient segments. To give you a little bit of color to first look at the hemodialysis population. We are getting inflamed hyporesponses and iron-deficient patients in hemodialysis. We have not seen a very large conversion for ESA-treated patients who are maintained properly and have performed well on ESAs. On peritoneal dialysis, however, because of the oral administration, we are seeing a lot of conversion patients as well as new patients, regardless of how they have responded to ESAs in the past. So I think in terms of differentiating the product profile, it's a very, very strong value proposition to hemodialysis and peritoneal dialysis, and that is the same in the case of non-dialysis as well.

Enrique A. Conterno

CEO & Director

Chris, maybe you can also comment about China has a uniquely large peritoneal dialysis patient population. Maybe you can comment about that.

Christine L. Chung

Senior Vice President of China Operations

Absolutely. So in terms of percentage right now, the peritoneal dialysis population is around 14% to 15%. The government is trying to increase it, but it's been stable at around that percentage. China currently has 800,000 dialysis patients, expected to exceed 1 million in the next couple of years. So if you just take 15% of 800,000 patients, there are currently over 100,000 peritoneal dialysis population patients in China. We've seen very, very strong adoption in both the installed base and new patients. And the initiation rate into PD is actually higher than hemodialysis. Interestingly, COVID has played a factor in it, because many new patients prefer to not be going to a hemodialysis center 3 times a week. Unexpected trend, of course, but very, very positive for adoption of roxadustat in China.

Enrique A. Conterno

CEO & Director

Very good. Thank you, Chris.

Operator

Your next question comes from Yaron Werber with Cowen.

Brendan Smith

Cowen and Company, LLC, Research Division

This is Brendan on for Yaron. Congrats on the progress. Just a couple of quick ones from us. First, I just really wanted to ask kind of about some of the top level kind of key learnings you've picked up from the China launch so far and how you're thinking about applying some of these to the U.S. launch, particularly in light of what's going on here and all the challenges, just kind of most important considerations you're bearing in mind. And then I also wanted to just quickly ask about the MDS and CIA trials. If you can give us any more granularity on where you're at in enrollment, respective time lines and when we might get some data from either of those?

Enrique A. Conterno

CEO & Director

Yes. Let me try to address your first question. I'm going to ask Peony to discuss both the MDS and the CIA trials. When it comes to learnings from China, as you can imagine, it's probably not in our best interest to be discussing those, given the competitive environment that we have in other markets. But I think it's fair to say, I think that one of the things that we've learned is that we have the ability to be able to grow roxadustat in different patient populations. I think this is important because it gives you a number of different ways to grow. And given when we think about hemodialysis, peritoneal dialysis, non-dialysis patients, it's just a broad spectrum of patients that can give us huge legs for growth into the future. So very excited about what that could do for us in the U.S. for us to think, yes, short-term, when it comes to the launch, but also longer-term in terms of what this product could become. And I'm going to ask Peony to give us an update now on both MDS and CIA.

K. Peony Yu

Chief Medical Officer

Thank you. Both the MDS and CIA trial are going well. The COVID inevitably has had some impact on some of the study sites. And -- but we were able to work with our investigators in ensuring patient safety while optimizing patient enrollment. At the same time, we have instituted remote monitoring process and remote data review to ensure data integrity. And we are not seeing increase in subject visits or during the pandemic because our investigators are managing the study so well. And we anticipate that with all the -- some of these adaptations and continued strong effort that these 2 studies will continue to be able to be executed successfully.

Enrique A. Conterno

CEO & Director

We feel good about our enrollment with both of those trials. Despite the impact, I think the team has appropriately adapted to ensure that we can enroll very well.

Operator

Your next question comes from Paul Choi with Goldman Sachs.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

A few for me, please. Enrique, maybe could you comment on how you see the role of roxa in the home dialysis setting here in the U.S.? Is that a commercial priority for you? And how are you thinking about potentially marketing to that market? Second, your partner presented updated NDD data from the DOLOMITES study at a recent medical meeting. I was just wondering if you could also maybe comment on your updated thoughts with regard to the MACE and MACE+ endpoints and how that adds to the totality of the existing CV data? And then third, given the uptick you've had in China so far, Enrique, how do you think about potentially unlocking shareholder value there from that business and either monetizing it or thinking about it potentially as a separate entity?

Enrique A. Conterno

CEO & Director

Yes. Very good. Let me try to have different people answer your -- the opportunities. Maybe on roxadustat and the opportunity in home dialysis, I'm going to ask Thane to maybe provide a few comments; on

DOLOMITES, I'll ask Peony to comment; and then I'll answer the question around China and unlocking shareholder value. Thane?

Thane Wettig

Chief Commercial Officer

Yes. Sure. As it relates to home dialysis, it's clearly not the priority segment as the LDO or the MDO or the other dialysis centers are the hospital-based dialysis centers. Same thing with the NDD population. We're taking a look at it right now to determine what level of presence we need in order to take advantage of that. But I think it's a different dynamic than it is in China.

Enrique A. Conterno

CEO & Director

Yes. We have clearly a very favorable product profile, but the relative size of the opportunity is smaller here than in China. Peony on NDD and DOLOMITES?

K. Peony Yu

Chief Medical Officer

Yes. So just on MDD DOLOMITES, we believe that this active control study of roxadustat being compared against darbepoetin provides further confidence on roxadustat. In that, we demonstrate efficacy in comparison to the active comparator. And importantly, the hazard ratio of MACE is 0.8. And so this is incremental confidence-building on top of the non-dialysis pool analysis.

Enrique A. Conterno

CEO & Director

Keep in mind, Paul, as we've shared before, I think there is agreement with the FDA on the studies that are the pivotal studies to be pooled for the MACE analysis in the U.S., DOLOMITES was not part of that. But of course, you see what the results are, and they are I think we can say encouraging.

When it comes to your question on unlocking value in China, the best way for us to ensure that we can lock as much value in China as possible is to make roxadustat as large as possible as we can. So for us, I think having a great launch I think is critical. Keep in mind that when we look at -- I'm going to mention this again, when we look at benchmarks of products that are innovative blockbusters in China, and when we look at either their revenue uptake or listing uptake, roxadustat studies comparing extremely well. So clearly, I think this is priority one. As I've mentioned, I think we are going to be looking at all opportunities for us to ensure that our China business is fully appreciated by our shareholders, given the huge value that we believe that we have there.

Operator

We have reached the end of the Q&A session. I will now turn the call over to Enrique Conterno for closing remarks.

Enrique A. Conterno

CEO & Director

Very good. I want to thank everyone for joining us on this earnings call. And once again, all of our collaborators, whether they are patients or health care professionals, investigators, regulators that are allowing us to progress our agenda. But in particular, I want to thank the entire FibroGen team for the commitment to the type of progress that we are seeing today. So thank you very much, everyone.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may now disconnect.

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EXHIBIT DD

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-Q

Mark			
	QUARTERLY REPORT PURSUAN 1934	TT TO SECTION 13 OR 15(d) OF THE S	ECURITIES EXCHANGE ACT OF
		For the quarterly period ended June 30, 2020	
		OR	
	TRANSITION REPORT PURSUAN 1934	TT TO SECTION 13 OR 15(d) OF THE S	SECURITIES EXCHANGE ACT OF
		r the transition period from to	
		Commission file number: 001-36740	
		FIBROGEN, INC.	
	(E 2	xact name of registrant as specified in its charter)	
	Delaware (State or Other Jurisdiction of Incorporation or Organization)		77-0357827 (I.R.S. Employer Identification No.)
	409 Illinois Street San Francisco, CA (Address of Principal Executive Office	es)	94158 (Zip Code)
		(415) 978-1200 Registrant's telephone number, including area code:	
:	Securities registered pursuant to Section 12		
	Title of each class	Trading Symbol	Name of each exchange on which registered
	Common Stock, \$0.01 par value	FGEN	The Nasdaq Global Select Market
.934 du equire 105 of 1	uring the preceding 12 months (or for such shoments for the past 90 days. Yes ☑ No ☐ Indicate by check mark whether the registrant	:: (1) has filed all reports required to be filed by Sectioner period that the registrant was required to file such that submitted electronically every Interactive Data in the preceding 12 months (or for such shorter per	ch reports), and (2) has been subject to such filing File required to be submitted pursuant to Rule
or an ei		is a large accelerated filer, an accelerated filer, a nor of "large accelerated filer," "accelerated filer," "small	
	Large accelerated filer \square Non-accelerated filer \square		Accelerated filer □ Smaller reporting company □ Emerging growth company □
		check mark if the registrant has elected not to use the ovided pursuant to Section 13(a) of the Exchange Act	
	Indicate by check mark whether the registrant The number of shares of common stock outsta	is a shell company (as defined in Exchange Act Rulanding as of July 31, 2020 was 90,355,096.	le 12b-2). Yes □ No ☑

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AstraZeneca Agreements

U.S./Rest of World ("RoW") Agreement

Effective July 30, 2013, the Company entered into a collaboration agreement with AstraZeneca AB ("AstraZeneca") for the development and commercialization of roxadustat for the treatment of anemia in the U.S. and all other countries in the world, other than China, not previously licensed under the Astellas Europe and Astellas Japan Agreements ("U.S./RoW Agreement"). It also excludes China, which is covered by a separate agreement with AstraZeneca described below. Under the terms of the U.S./RoW Agreement, AstraZeneca paid upfront, non-contingent, non-refundable and time-based payments totaling \$374.0 million (such amounts were fully received as of June 2016). Under the U.S./RoW Agreement, the Company is also eligible to receive from AstraZeneca an aggregate of approximately \$875.0 million in potential milestone payments, comprised of (i) up to \$65.0 million in milestone payments upon achievement of specified clinical and development milestone events, \$15.0 million of which was received in 2015 as a result of the finalization of its two audited pre-clinical carcinogenicity study reports, and the remaining \$50.0 million was received in April 2020 as a result of the NDA submission milestone, (ii) up to \$325.0 million in milestone payments upon achievement of specified regulatory milestone events, (iii) up to \$160.0 million in milestone payments related to activity by potential competitors and (iv) up to approximately \$325.0 million in milestone payments upon the achievement of specified commercial sales events. The aggregate amount of consideration received through June 30, 2020 totals \$439.0 million.

As mentioned above, during the second quarter of 2019, the Company received positive topline results from analyses of pooled MACE and MACE+ data from its Phase 3 trials for roxadustat, enabling the Company's NDA submission to the FDA. The regulatory milestone payment associated with this NDA submission became probable of being achieved in the second quarter of 2019. Accordingly, the consideration of \$50.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the U.S./ RoW Agreement in the second quarter of 2019, of which \$42.4 million was recognized as revenue during 2019, and \$0.4 million was recognized as revenue during the six months ended June 30, 2020, from performance obligations satisfied or partially satisfied. The Company submitted such NDA in December 2019, which was accepted by the FDA for review in February 2020. According to the U.S/RoW Agreement, this milestone payment is billable to AstraZeneca when the NDA is accepted by the FDA. Therefore this \$50.0 million was billed during the first quarter of 2020, the payment of which was fully received in April 2020.

China Agreement

Effective July 30, 2013, the Company (through its subsidiaries affiliated with China) entered into a collaboration agreement with AstraZeneca for the development and commercialization (but not manufacture) of roxadustat for the treatment of anemia in China ("China Agreement"). Under the terms of the China Agreement, AstraZeneca agreed to pay upfront consideration totaling \$28.2 million (such amounts were fully received in 2014). Under the China Agreement, the Company is also eligible to receive from AstraZeneca an aggregate of approximately \$348.5 million in potential milestone payments, comprised of (i) up to \$15.0 million in milestone payments upon achievement of specified regulatory milestone events, and (iii) up to approximately \$187.5 million in milestone payments upon the achievement of specified commercial sales and other events. The China Agreement is structured as a 50/50 profit or loss share (as defined) and provides for joint development costs (including capital and equipment costs for construction of the manufacturing plant in China), to be shared equally during the development. The aggregate amount of such consideration received through June 30, 2020 totals \$77.2 million.

In December 2019, roxadustat was included on the updated National Reimbursement Drug List ("NRDL") released by China's NHSA for the treatment of anemia in CKD, covering patients who are non-dialysis dependent as well as those who are dialysis-dependent. The inclusion on the NRDL triggered a total of \$22.0 million milestones payable to the Company by AstraZeneca. Accordingly, the total consideration of \$22.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the China Agreement during fourth quarter of 2019. This milestone payment was received during the first quarter of 2020.

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AstraZeneca and Astellas approved the development of roxadustat for the treatment of chemotherapy-induced anemia in December 2018 and January 2019, respectively. Costs associated with the development of this indication are expected to be shared 50/50 between AstraZeneca and Astellas. In addition, in December 2018, anemia of chronic inflammation and multiple myeloma was approved for development by AstraZeneca and is expected to be fully funded by them. For revenue recognition purposes, the Company concluded that the addition of these new indications represents a modification to the collaboration agreements and will be accounted for separately, meaning the development costs associated with the new indications are distinct from the original development costs. The development service period for roxadustat for the treatment of chemotherapy-induced anemia, anemia of chronic inflammation and multiple myeloma under the AstraZeneca agreements is estimated to continue through the end of 2024, to allow for development of these additional indications.

On July 8, 2020, FibroGen Cayman, FibroGen Beijing and FibroGen International (Hong Kong) Limited (collectively, "FibroGen China") and AstraZeneca (together with FibroGen China, the "Parties") entered into an amendment, effective July 1, 2020, to the China Agreement, relating to the development and commercialization of roxadustat in China. See Note 10 for details.

Summary of Revenue Recognized Under the Collaboration Agreements

The table below summarizes the accounting treatment for the various performance obligations pursuant to each of the Astellas and AstraZeneca agreements. License amounts identified below are included in the "License revenue" line item in the condensed consolidated statements of operations. All other elements identified below are included in the "Development and other revenue" line item in the condensed consolidated statements of operations.

Amounts recognized as revenue under the Japan Agreement were as follows (in thousands):

			Three Months	Ended	l June 30,	 Six Months Ended June 30,			
Agreement	Performance Obligation		2020		2019	2020	2019		
Japan	License revenue	\$	_	\$	_	\$ _	\$	_	
	Development revenue	\$	164	\$	369	\$ 327	\$	615	

The transaction price related to consideration received and accounts receivable has been allocated to each of the following performance obligations under the Japan Agreement, along with any associated deferred revenue as follows (in thousands):

Japan Agreement	Cumulative Revenue Through June 30, 2020	Deferred Revenue at June 30, 2020	Total Consideration Through June 30, 2020		
License	\$ 86,024	\$ _	\$	86,024	
Development revenue	15,458	183		15,641	
Total license and development revenue	\$ 101,482	\$ 183	\$	101,665	

The revenue recognized under the Japan Agreement for the three months ended June 30, 2020 included an increase in revenue of \$0.1 million resulting from changes to estimated variable consideration in the current period relating to performance obligations satisfied or partially satisfied in previous periods. The remainder of the transaction price related to the Japan Agreement includes no further variable consideration from estimated future co-development billing.

Amounts recognized as revenue under the Europe Agreement were as follows (in thousands):

		 Three Month	ıs Ended	1 June 30,	Six Months Ended June 30,				
Agreement	Performance Obligation	2020		2019	2020		2019		
Europe	License revenue	\$ _	\$	117,470	\$	_	\$	117,470	
	Development revenue	\$ 4,602	\$	16,854	\$	9,176	\$	21,467	

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The transaction price related to consideration received and accounts receivable has been allocated to each of the following performance obligations under the Europe Agreement, along with any associated deferred revenue as follows (in thousands):

Europe Agreement	umulative Revenue Through ne 30, 2020	R	Deferred evenue at ne 30, 2020	Total nsideration Through ne 30, 2020
License	\$ 487,951	\$	_	\$ 487,951
Development revenue	240,184		2,338	242,522
Total license and development revenue	\$ 728,135	\$	2,338	\$ 730,473

The revenue recognized under the Europe Agreement for the three months ended June 30, 2020 included an increase in revenue of \$1.6 million resulting from changes to estimated variable consideration in the current period relating to performance obligations satisfied or partially satisfied in previous periods. The remainder of the transaction price related to the Europe Agreement includes \$31.7 million of variable consideration from estimated future codevelopment billing and is expected to be recognized over the remaining development service period.

Amounts recognized as revenue under the U.S./RoW Agreement were as follows (in thousands):

		 Three Months	Ended Ju	ne 30,	Six Months Ended June 30,					
Agreement	Performance Obligation	2020		2019		2020		2019		
U.S. / RoW and China	License revenue	\$ _	\$	33,111	\$	_	\$	33,111		
	Development revenue	13,750		23,762		28,305		42,766		
	China performance obligation	\$ 441	\$	_	\$	594	\$	_		

The transaction price related to consideration received and accounts receivable has been allocated to each of the following performance obligations under the U.S./RoW Agreement and China Agreement, along with any associated deferred revenue as follows (in thousands):

U.S. / RoW and China Agreements	umulative Revenue Through ne 30, 2020	R	Deferred evenue at ne 30, 2020	Total Consideration Through June 30, 2020		
License	\$ 341,844	\$	_	\$	341,844	
Co-development, information sharing &						
committee services	521,572		4,547		526,119	
China performance obligation	684		140,973		141,657	
Total license and development revenue	\$ 864,100	\$	145,520	\$	1,009,620	

The revenue recognized under the U.S./RoW Agreement for the three months ended June 30, 2020 included a decrease of \$0.2 million in revenue resulting from changes to estimated variable consideration in the current period relating to performance obligations satisfied or partially satisfied in previous periods. The remainder of the transaction price related to the U.S./RoW Agreement and China Agreement includes \$90.1 million of variable consideration from estimated future co-development billing and is expected to be recognized over the remaining development service period, except for amounts allocated to the China performance obligation, which are expected to be recognized in a pattern consistent with estimated deliveries of the commercial drug product.

Product Revenue, Net

The Company started roxadustat commercial sales in China in the third quarter of 2019. Product revenue is recognized in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those products, net of various sales rebates and discounts. Product revenue, net was as follows (in thousands):

	 e Months Ended une 30, 2020	Six Months Ended June 30, 2020			
Gross revenue	\$ 19,833	\$	25,205		
Non-key account hospital listing award	(2,566)		(2,566)		
Contractual sales rebate	(1,372)		(1,748)		
Other discounts and rebates	(202)		(243)		
Product revenue, net	\$ 15,693	\$	20,648		

In the second quarter of 2020, the Company amended the agreement with its pharmaceutical distributors, which triggered accounting modifications particularly related to non-key account hospital listing award. During the three months ended June 30, 2020, a \$2.6 million of non-key account hospital listing award was recorded as a reduction to the revenue, which was calculated based on eligible non-key account hospital listing to date achieved by each distributor with certain requirements met during the period.

For the three and six months ended June 30, 2020, the contractual sales rebate was \$1.4 million and \$1.7 million, respectively, which were calculated based on the stated percentage of gross sales by each distributor in the distribution agreement entered between FibroGen and each distributor. All other rebates and discounts, including sales return allowance were immaterial for the period.

The rebates and discounts that the Company's pharmaceutical distributors have earned are eligible to be applied against their future sales order, limited to certain maximums until such rebates and discounts are exhausted. These rebates and discounts are recorded as contract liabilities at the time they become eligible in the same period that the related revenue is recorded. Due to the distributor's legal right to offset, at each balance sheet date, the rebates and discounts are presented as reductions to gross accounts receivable from the distributor, or as a current liability to the distributor to the extent that the total amount exceeds the gross accounts receivable. The distributor's legal right of offset is calculated at the individual distributor level. The following table includes a roll-forward of the contract liabilities (in thousands):

												sented Net		
	Balance at December 31, 2019						Currency Gross Contract Translation Liabilities			_	Against .ccounts	Ralan	ce at June	
			Additions		Deduction		and Other		Balance		Receivable		30, 2020	
Contract liabilities	\$	(1,102)	\$	(4,907)	\$	16	\$	9	\$	(5,984)	\$	5,595	\$	(389)

Palance

As of June 30, 2020, the total rebates and discounts as reductions to gross accounts receivable was \$5.6 million, and the total contract liabilities was \$0.4 million, which was included in accrued and other current liabilities in the condensed consolidated balance sheet.

The above-mentioned contra-accounts receivable items related to product revenue consisted of the following (in thousands):

	J	June 30, 2020	December 31, 2019			
Price adjustment	\$	935	\$ 936			
Contractual sales rebate		1,878	148			
Non-key account hospital listing award		2,567	_			
Other discounts and rebates		260	18			
Provision for credit loss		84	_			
Total reductions to gross accounts receivable	\$	5,724	\$ 1,102			

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ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.

You should read the following discussion and analysis of our financial condition and results of operations in conjunction with the condensed consolidated financial statements and the notes thereto included elsewhere in this Quarterly Report on Form 10-Q, and in our Securities and Exchange Commission ("SEC") filings, including our Annual Report on Form 10-K for the year ended December 31, 2019 filed with the SEC on March 2, 2020.

FORWARD-LOOKING STATEMENTS

The following discussion and information contained elsewhere in this Quarterly Report on Form 10-Q contain "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended ("Exchange Act"), Section 27A of the Securities Act of 1933, as amended ("Securities Act") and within the meaning of the Private Securities Litigation Reform Act of 1995. These statements are often identified by the use of words such as "may," "will," "expect," "believe," "anticipate," "intend," "could," "should," "estimate," or "continue," and similar expressions or variations. Such forward-looking statements are subject to risks, uncertainties and other factors that could cause actual results and the timing of certain events to differ materially from future results expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section titled "Risk Factors," set forth in Part II, Item 1A of this Quarterly Report on Form 10-Q. The forward-looking statements in this Quarterly Report on Form 10-Q represent our views as of the date of this Quarterly Report on Form 10-Q. We anticipate that subsequent events and developments will cause our views to change. New risks emerge from time to time, and it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties, and assumptions, the forward-looking events and circumstances discussed in this Quarterly Report on Form 10-Q may not occur, and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. While we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this Quarterly Report on Form 10-Q and are cautioned not to place undue reliance on such forward-looking statements.

BUSINESS OVERVIEW

We were incorporated in 1993 in Delaware and are headquartered in San Francisco, California, with subsidiary offices in Beijing and Shanghai, People's Republic of China ("China"). We are a leading biopharmaceutical company developing and commercializing a pipeline of first-in-class therapeutics. We apply our pioneering expertise in hypoxia-inducible factor ("HIF"), connective tissue growth factor ("CTGF") biology, and clinical development to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer.

Roxadustat, our most advanced product, is an oral small molecule inhibitor of HIF prolyl hydroxylase ("HIF-PH") activity that has received marketing authorization in China for the treatment of anemia caused by chronic kidney disease ("CKD") in dialysis and non-dialysis patients. Evrenzo® (roxadustat) is approved in Japan for the treatment of anemia associated with CKD in dialysis patients. In January 2020, Astellas Pharma Inc. ("Astellas") submitted a supplemental New Drug Application ("NDA") in Japan for the treatment of anemia in non-dialysis CKD patients.

Our NDA filing in the United States ("U.S.") for roxadustat for the treatment of anemia in dialysis and non-dialysis CKD patients was accepted by the U.S. Food and Drug Administration ("FDA") in February 2020. In Europe, the Marketing Authorization Application ("MAA") filing for roxadustat for the treatment of anemia in dialysis and non-dialysis CKD patients was accepted for regulatory review by the European Medicines Agency ("EMA") in May 2020.

Roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes ("MDS"). Roxadustat is in Phase 2 clinical development for chemotherapy-induced anemia.

Pamrevlumab, an anti-CTGF human monoclonal antibody, is in Phase 3 clinical development for the treatment of both idiopathic pulmonary fibrosis ("IPF") and pancreatic cancer. Pamrevlumab is also currently in a Phase 2 trial for Duchenne muscular dystrophy ("DMD") and is in Phase 2/3 development in Severe Acute Respiratory Syndrome Coronavirus 2019 Disease ("COVID-19").

Impact of COVID-19

On March 11, 2020, COVID-19, a disease caused by a novel strain of the coronavirus, was characterized as a pandemic by the World Health Organization. Since December 2019, COVID-19 has spread rapidly. The rapid spread has resulted in authorities implementing numerous measures to contain the virus, such as travel restrictions, social distancing requirements, quarantines, shelter-in-place orders or voluntarily adopted practices, and business shutdowns.

We have taken measures to minimize the health risks of COVID-19 to our staff, patients, healthcare providers and their communities, as their safety and well-being are our top priority. In the U.S., our employees are working remotely when possible, while in China they have returned to work in our offices, manufacturing plants, and are performing medical affairs out in the field. While we have seen some impacts from COVID-19, such as slower enrollment in our clinical trials and some effect on our roxadustat sales in China, particularly in February and March, we do not know if, or to what extent, these effects will continue in the future, as the impact of the COVID-19 pandemic continues to unfold. The effect on our operational and financial performance will depend in large part on future developments with the disease, which cannot be predicted with confidence at this time. Future developments include the duration, scope, and severity of the COVID-19 pandemic, the actions taken to contain or mitigate its impact, the impact on governmental programs and budgets, the impact on healthcare systems and operating procedures, the development of treatments or vaccines, and the resumption of widespread economic activity. Due to the inherent uncertainty of the largely unprecedented and rapidly evolving situation, we are unable to predict with any confidence the likely impact of the COVID-19 pandemic on our future operations.

The financial results for the three months ended June 30, 2020 were not significantly impacted by COVID-19 relative to prior quarters. However, we will continue to monitor, and to the extent possible, mitigate the impact of the COVID-19 pandemic on our business.

Financial Highlights

Three Months Ended June 30,				Six Months Ended June 30,			
	2020		2019		2020		2019
(in thousands, except for per share data)							
\$	42,888	\$	191,566	\$	67,288	\$	215,429
	128,025		78,747		233,500		151,453
	(85,313)		116,003		(163,661)		70,592
	(0.95)		1.34		(1.84)		0.82
\$	(0.95)	\$	1.26	\$	(1.84)	\$	0.77
	\$	\$ 42,888 128,025 (85,313) (0.95)	\$ 42,888 \$ 128,025 (85,313)	\$ 42,888 \$ 191,566 128,025 78,747 (85,313) 116,003 (0.95) 1.34	2020 2019 (in thousands, except for p \$ 42,888 \$ 191,566 \$ 128,025 78,747 (85,313) \$ 116,003 \$ (0.95) \$ 1.34	2020 2019 2020 (in thousands, except for per share data) \$ 42,888 191,566 67,288 128,025 78,747 233,500 (85,313) 116,003 (163,661) (0.95) 1.34 (1.84)	2020 2019 2020 (in thousands, except for per share data) \$ 42,888 \$ 191,566 \$ 67,288 \$ 128,025 78,747 233,500 \$ (85,313) 116,003 (163,661) (0.95) 1.34 (1.84)

	Ju	June 30, 2020		ember 31, 2019	
		(in thousands)			
Balance Sheet					
Cash and cash equivalents	\$	429,269	\$	126,266	
Short-term and long-term investments		256,546		468,609	
Accounts receivable	\$	26,519	\$	28,455	

Our revenue for the three and six months ended June 30, 2020 included the revenue recognized related to the following:

- \$19.0 million and \$38.4 million of development revenue recognized under our collaboration agreements with our partners Astellas and AstraZeneca AB ("AstraZeneca");
- \$15.7 million and 20.6 million of net product revenue from roxadustat commercial sales in China; and
- \$8.2 million of roxadustat active pharmaceutical ingredient ("API") delivery to Astellas.

As comparison, our revenue for the three and six months ended June 30, 2019 included the revenue recognized related to the following:

- Two regulatory milestones totaling \$130.0 million associated with the MAA submission to the EMA under the collaboration agreement with Astellas for roxadustat as a treatment for dialysis and non-dialysis CKD patients;
- A \$50.0 million regulatory milestone associated with the NDA submission to the FDA under the collaboration agreement with AstraZeneca for roxadustat as a treatment for dialysis and non-dialysis CKD patients; and
- Development revenue recognized under our collaboration agreements with Astellas and AstraZeneca.

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Operating costs and expenses for the three and six months ended June 30, 2020 increased compared to the same periods a year ago primarily due to the following:

- Higher outside service expenses associated with co-promotional activities expenses with AstraZeneca sales and marketing efforts in China related to
 the commercial activities of roxadustat;
- Higher clinical trial expenses associated with post-approval safety studies in China, and commencement of Phase 3 trials for pamrevlumab, offset by lower activities due to substantial completion of Phase 3 trials for roxadustat;
- Higher legal expenses primarily associated with patent-related activities in the United Kingdom;
- · Higher employee-related expenses resulting from higher average compensation level and headcount; and
- Higher drug development expenses mainly associated with higher drug substance manufacturing activities and supplies related to pamrevlumab, and higher drug substance manufacturing activities related to roxadustat in its global program.

During the three months ended June 30, 2020, we had a net loss of \$85.3 million, or net loss per basic and diluted share of \$0.95, as compared to a net income of \$116.0 million for the same period a year ago, due to a decrease in revenue and an increase in operating costs and expenses. During the six months ended June 30, 2020, we had a net loss of \$163.7 million, or net loss per basic and diluted share of \$1.84, as compared to a net income of \$70.6 million for the same period a year ago, due to a decrease in revenue and an increase in operating costs and expenses.

Cash and cash equivalents, investments and accounts receivable totaled \$712.3 million at June 30, 2020, an increase of \$89.0 million from December 31, 2019, primarily due to the cash provided by operations.

Commercial and Development Programs

Roxadustat for the Treatment of Anemia in Chronic Kidney Disease

Roxadustat is our most advanced product, an oral small molecule inhibitor of HIF-PH activity that acts by stimulating the body's natural pathway of erythropoiesis, or red blood cell production.

We continue our commercial launch efforts for roxadustat (tradename: 爱瑞卓®) in China after receiving marketing authorization for the treatment of anemia caused by CKD in non-dialysis and dialysis patients. Roxadustat was added to the National Reimbursement Drug List ("NRDL"), effective January 1, 2020. Now that China has largely re-opened, we and our partner AstraZeneca continue our strong focus on hospital listings for roxadustat. As of the end of the second quarter, roxadustat was listed at hospitals which represent approximately 45% of the CKD anemia market opportunity in China.

In Japan, our partner Astellas continues the commercial launch of Evrenzo® (roxadustat), which was approved for the treatment of anemia associated with CKD in dialysis patients. In January 2020, Astellas submitted a supplemental NDA in Japan for the treatment of anemia in CKD patients not on dialysis. This supplemental NDA is under review by the Pharmaceuticals and Medical Devices Agency for the use of roxadustat in patients with anemia of CKD not on dialysis, with an anticipated approval decision expected by year-end.

In conjunction with our collaboration partners, AstraZeneca and Astellas, we have completed the Phase 3 trials of roxadustat supporting our NDA in the U.S. and the MAA in the European Union and the United Kingdom (collectively, "Europe") for the treatment of anemia in CKD.

With respect to our U.S. NDA, we completed our mid-cycle review meeting with the FDA in June 2020 and continue to expect an FDA decision on this NDA by the Prescription Drug User Fee Act goal date of December 20, 2020. The FDA has indicated that an Advisory Committee meeting is not planned at this time.

In May 2020, our partner Astellas' MAA for roxadustat for the treatment of anemia in patients with CKD was accepted for regulatory review by the EMA. Our partner Astellas expects an approval decision by the EMA in the middle of 2021.

In addition, in collaboration with AstraZeneca, applications for marketing authorization of roxadustat in CKD anemia have been submitted for Canada, Australia, Mexico, Brazil, Chile, Taiwan, South Korea, Philippines, Singapore, and India.

During the second quarter of 2020, we announced data from roxadustat clinical trials conducted by Astellas. These data were presented in virtual oral sessions of the 57th European Renal Association-European Dialysis and Transplant Association.

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The Phase 3 DOLOMITES study evaluated the efficacy and safety of roxadustat compared to darbepoetin alfa for the treatment of anemia in non-dialysis dependent patients. In the primary endpoint analysis, the study demonstrated non-inferiority of roxadustat to darbepoetin alfa in the proportion of patients achieving correction of hemoglobin (Hb) levels during the first 24 weeks of treatment (89.5% vs 78.0%; a difference of 11.51%), with a lower bound of 95% confidence interval > 0%.

Roxadustat was superior to darbepoetin alfa in decreasing low-density lipoprotein cholesterol with a least square mean (LSM) difference of -0.403 mmol/L (p<0.01) and superior in time to first intravenous iron use with a hazard ratio (HR) of 0.45 (95% CI: 0.26, 0.78; p=0.004). The non-inferiority of roxadustat to darbepoetin alfa on hypertension risk was demonstrated for mean arterial pressure change from baseline to weeks 12-28 with a LSM difference of -0.372 mmHg (95% CI: -1.587, 0.842) and time to occurrence of hypertension; HR 0.83 (95% CI: 0.56, 1.22). Regarding safety, the overall incidence of treatment-emergent adverse events was comparable between roxadustat and darbepoetin alfa (91.6% and 92.5%, respectively).

With a relatively small sample size (roxadustat n=323, darbepoetin n=293), non-confirmatory analysis of adjudicated major adverse cardiac events ("MACE"), and MACE plus hospitalized unstable angina and hospitalized congestive heart failure ("MACE+") outcomes showed HR point estimates of 0.81 (95% CI: 0.52, 1.25) and 0.90 (95% CI: 0.61, 1.32) for roxadustat as compared to darbepoetin.

Roxadustat for the Treatment of Chemotherapy-Induced Anemia

We continue to enroll our Phase 2 clinical trial of roxadustat in the U.S. in chemotherapy-induced anemia. This is a single-arm open label study investigating the efficacy and safety of roxadustat for the treatment of anemia in up to 100 patients receiving myelosuppressive chemotherapy treatment for non-myeloid malignancies, with a treatment duration of 16 weeks.

Roxadustat for the Treatment of Anemia in Myelodysplastic Syndromes

We are continuing to enroll our global 160-patient double-blind, placebo-controlled Phase 3 clinical study of roxadustat in transfusion-dependent, lower risk MDS patients. Patients are randomized 3:2 to receive roxadustat or placebo three-times-weekly. The primary endpoint is the proportion of patients who achieve 8-week transfusion independence by 28 weeks with safety evaluated up to 52 weeks.

In China, the Phase 2/3 clinical trial to evaluate the safety and efficacy of roxadustat in non-transfusion dependent, lower risk MDS patients with anemia is ongoing.

Pamrevlumab (FG-3019) - Monoclonal Antibody Against Connective Tissue Growth Factor (CTGF)

Pamrevlumab is our human monoclonal antibody that inhibits the activity of CTGF, a central mediator and critical common element in the progression of fibrotic and fibro-proliferative diseases.

In the U.S., the FDA has granted Orphan Drug Designation to pamrevlumab for the treatment of IPF, locally advanced unresectable pancreatic cancer, and DMD. Pamrevlumab has also received Fast Track designation from the FDA for the treatment of both IPF and locally advanced unresectable pancreatic cancer.

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Severe Acute Respiratory Syndrome Coronavirus 2019 Disease ("COVID-19")

In June 2020, we announced initiation of an open-label, randomized, parallel-arm study investigating the efficacy and safety of pamrevlumab versus standard of care in patients with COVID-19 infection in Italy. This study is a Phase 2/3 investigator-initiated clinical trial investigating the efficacy and safety of pamrevlumab in approximately 68 patients hospitalized with COVID-19. The primary objective of this study is to assess the effect of pamrevlumab on blood oxygenation in patients with COVID-19 infection. Patients will be randomized to treatment with pamrevlumab or standard of care in a 1:1 ratio. Based on the investigator's decision, a subgroup of patients may continue treatment for up to 12 weeks.

We have also initiated a randomized, double-blind, placebo-controlled Phase 2 study investigating the efficacy and safety of pamrevlumab in hospitalized patients with acute COVID-19 infection in the U.S. This multicenter trial will enroll approximately 130 patients with COVID-19. The primary objective of this study is to assess the effect of pamrevlumab on blood oxygenation in patients with COVID-19 infection, and patients will be randomized to treatment with pamrevlumab or standard of care in a 1:1 ratio. The primary efficacy assessment is the proportion of hospitalized COVID-19 patients who have not received mechanical ventilation and/or extracorporeal membrane oxygenation (ECMO) and remain alive at Day 28.

Idiopathic Pulmonary Fibrosis

We are conducting ZEPHYRUS, our Phase 3 trial of pamrevlumab in IPF patients, and are preparing to initiate ZEPHYRUS-2, a second IPF Phase 3 study. Both studies are double-blind, placebo-controlled Phase 3 trials targeting approximately 340 patients with a primary U.S. efficacy endpoint of change from baseline in forced vital capacity. In order to minimize the risk of exposure to COVID-19 in this vulnerable IPF patient population with compromised lung function, we paused enrollment in ZEPHYRUS in the first quarter of 2020. We have now re-opened enrollment in ZEPHYRUS and will initiate the ZEPHYRUS-2 trial as COVID-19 conditions improve.

Locally Advanced Unresectable Pancreatic Cancer

In 2019, we initiated LAPIS, our double-blind placebo controlled Phase 3 clinical program for pamrevlumab as a neoadjuvant therapy for locally advanced unresectable pancreatic cancer. We intend to enroll approximately 260 patients, randomized at a 1:1 ratio to receive either pamrevlumab or placebo, in each case in combination with gemcitabine and nab-paclitaxel. We are working with clinical trial sites and investigators in order to mitigate risks and other challenges associated with COVID-19 and the restrictions instituted to combat COVID-19.

Duchenne Muscular Dystrophy

In the third quarter of 2020, we expect to initiate a Phase 3 clinical trial, LELANTOS, evaluating pamrevlumab as a treatment for DMD. LELANTOS will be a double-blind, placebo-controlled trial in approximately 90 non-ambulatory DMD patients. Patients will be randomized at a 1:1 ratio to pamrevlumab or placebo and have a treatment period of 52 weeks. The primary endpoint will assess change in upper limb strength and additional endpoints will include pulmonary, performance, cardiac, and fibrosis assessments.

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Collaboration Partnerships for Roxadustat

Our current and future research, development, manufacturing and commercialization efforts with respect to roxadustat and our other product candidates currently in development depend on funds from our collaboration agreements with Astellas and AstraZeneca as described below.

Astellas

In June 2005, we entered into a collaboration agreement with Astellas for the development and commercialization (but not manufacture) of roxadustat for the treatment of anemia in Japan ("Japan Agreement"). In April 2006, we entered into the Europe Agreement with Astellas for roxadustat for the treatment of anemia in Europe, the Commonwealth of Independent States, the Middle East, and South Africa. Under these agreements, we provide Astellas the right to develop and commercialize roxadustat for anemia indications in these territories.

We share responsibility with Astellas for clinical development activities required for the U.S. and the EU regulatory approval of roxadustat and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will own and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements.

The Astellas agreements will continue in effect until terminated. Either party may terminate the agreements for certain material breaches by the other party. In addition, Astellas will have the right to terminate the agreements for certain specified technical product failures, upon generic sales reaching a particular threshold, upon certain regulatory actions, or upon our entering into a settlement admitting the invalidity or unenforceability of our licensed patents. Astellas may also terminate the agreements for convenience upon advance written notice to us. In the event of any termination of the agreements, Astellas will transfer and assign to us the regulatory filings for roxadustat and will assign or license to us the relevant trademarks used with the products in the Astellas territories. Under certain terminations, Astellas is also obligated to pay us a termination fee.

Consideration under these agreements includes a total of \$360.1 million in upfront and non-contingent payments, and milestone payments totaling \$557.5 million, of which \$542.5 million are development and regulatory milestones and \$15.0 million are commercial-based milestones. Total consideration, excluding development cost reimbursement and product sales-related payments, could reach \$917.6 million. The aggregate amount of such consideration received through June 30, 2020 totals \$630.1 million. Additionally, under these agreements, Astellas pays 100% of the commercialization costs in its territories. Astellas will pay us a transfer price, based on net sales, in the low 20% range for our manufacture and delivery of roxadustat.

During the second quarter of 2019, we received positive topline results from analyses of pooled MACE and MACE+ data from its Phase 3 trials evaluating roxadustat as a treatment for dialysis and non-dialysis CKD patients, enabling Astellas to prepare for an MAA submission to the EMA, following our NDA submission to the FDA in 2019. These milestones became probable of being achieved in the second quarter of 2019, and substantially all of the total consideration of \$130.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the Europe Agreement in the second quarter of 2019, of which \$128.8 million was recognized as revenue during 2019, and \$0.6 million was recognized as revenue during the six months ended June 30, 2020, from performance obligations satisfied or partially satisfied. According to the Europe Agreement, these milestone payments were billed to Astellas upon the submission of an MAA in the second quarter of 2020 and the total \$130.0 million was received during the same quarter.

In addition, as of June 30, 2020, Astellas had separate investments of \$80.5 million in the equity of FibroGen, Inc.

AstraZeneca

In July 2013, we entered into the U.S./RoW Agreement, a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in the U.S. and all territories not previously licensed to Astellas, except China. In July 2013, through our China subsidiary and related affiliates, we entered into the China Agreement, a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in China. Under these agreements, we provide AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories. We share responsibility with AstraZeneca for clinical development activities required for U.S. regulatory approval of roxadustat.

In 2015, we reached the \$116.5 million cap on our initial funding obligations (during which time we shared 50% of the joint initial development costs), therefore all development and commercialization costs for roxadustat for the treatment of anemia in CKD in the U.S., Europe, Japan and all other markets outside of China have been paid by Astellas and AstraZeneca since reaching the cap.

In China, FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") will conduct the development work for CKD anemia, will hold all of the regulatory licenses issued by China regulatory authorities, and will be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is also responsible for 100% of development expenses in all other licensed territories outside of China. Outside of China, we are responsible, through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the AstraZeneca agreements.

Under the AstraZeneca agreements, we will receive upfront and subsequent non-contingent payments totaling \$402.2 million. Potential milestone payments under the agreements total \$1.2 billion, of which \$571.0 million are development and regulatory milestones and \$652.5 million are commercial-based milestones. Total consideration under the agreements, excluding development cost reimbursement, transfer price payments, royalties and profit share, could reach \$1.6 billion. The aggregate amount of such consideration received through June 30, 2020 totals \$516.2 million.

Under the U.S./RoW Agreement, AstraZeneca will pay for all commercialization costs in the U.S. and RoW and AstraZeneca will be responsible for the U.S. commercialization of roxadustat, with FibroGen undertaking specified promotional activities in the end-stage renal disease segment in the U.S. In addition, we will receive a transfer price for delivery of commercial product based on a percentage of net sales in the low- to mid-single digit range and AstraZeneca will pay us a tiered royalty on net sales of roxadustat in the low 20% range.

Under the China Agreement, which is conducted through FibroGen China Anemia Holdings, Ltd., FibroGen Beijing, and FibroGen International (Hong Kong) Limited (collectively, ("FibroGen China"), the commercial collaboration is structured as a 50/50 profit share. AstraZeneca will conduct commercialization activities in China and fund roxadustat launch costs in China and will only receive reimbursement once FibroGen Beijing has achieved profitability. As of June 30, 2020, we accrued \$116.2 million of cumulative co-promotional expenses related to the estimated amount payable to AstraZeneca for such sales and marketing efforts.

Payments under these agreements include over \$500.0 million in upfront, non-contingent and other payments received or expected to be received prior to the first U.S. approval, excluding development expense reimbursement.

AstraZeneca may terminate the U.S./RoW Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon 180 days prior written notice at will. If AstraZeneca terminates the U.S./RoW Agreement at will, in addition to any unpaid non-contingent payments, it will be responsible for paying for a substantial portion of the post-termination development costs under the agreed development plan until regulatory approval.

AstraZeneca may terminate the China Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon advance prior written notice at will. If AstraZeneca terminates our China Agreement at will, it will be responsible for paying for transition costs as well as make a specified payment to FibroGen China.

In the event of any termination of the agreements, but subject to modification upon termination for technical product failure, AstraZeneca will transfer and assign to us any regulatory filings and approvals for roxadustat in the affected territories that they may hold under our agreements, grant us licenses and conduct certain transition activities.

As mentioned above, during the second quarter of 2019, we received positive topline results from analyses of pooled MACE and MACE+ data from its Phase 3 trials for roxadustat, enabling our NDA submission to the FDA. The regulatory milestone payment associated with this NDA submission became probable of being achieved in the second quarter of 2019. Accordingly, the consideration of \$50.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the U.S./ RoW Agreement in the second quarter of 2019, of which \$42.4 million was recognized as revenue during 2019, and \$0.4 million was recognized as revenue during the six months ended June 30, 2020, from performance obligations satisfied or partially satisfied. We submitted such NDA in December 2019, which was accepted by the FDA for review in February 2020. According to the U.S/RoW Agreement, this milestone payment is billable to AstraZeneca when the NDA is accepted by the FDA. Therefore, this \$50.0 million milestone was billed during the first quarter of 2020, the payment of which was fully received in April 2020.

In December 2019, roxadustat was included on the updated NRDL released by China's National Healthcare Security Administration for the treatment of anemia in CKD, covering patients who are non-dialysis-dependent as well as those who are dialysis-dependent. The inclusion on the NRDL triggered a total of \$22.0 million milestones payable to us by AstraZeneca. Accordingly, the total consideration of \$22.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the U.S./ RoW Agreement in the fourth quarter of 2019. This milestone payment was fully received during the first quarter of 2020.

On July 8, 2020, FibroGen China and AstraZeneca (together with FibroGen China, the "Parties") entered into an amendment, effective July 1, 2020, to the China Agreement, relating to the development and commercialization of roxadustat in China (the "Amendment").

The Amendment provides for the establishment of a jointly owned entity (the "Distribution Entity") that will perform roxadustat distribution, as well as conduct sales and marketing through AstraZeneca. FibroGen Beijing will continue to hold all of the regulatory licenses issued by China regulatory authorities and will continue to be primarily responsible for regulatory, clinical, manufacturing, medical affairs and pharmacovigilance. In July 2020, the Company closed the acquisition of an entity for the purpose of the establishment of the Distribution Entity.

While the responsibilities of the Parties under the China Agreement remain largely the same, certain changes are being made. The Parties have changed the method under which commercial expenses are billed, and the collaboration will be adjusted to more fully account for the cost of manufacturing. These changes will be implemented retroactively to April 1, 2020. AstraZeneca's billings for sales and marketing are now subject to an annual cap at a percentage of net sales, until they have been fully reimbursed for their costs, at which point AstraZeneca will invoice based on actual costs, subject to the annual cap.

Once the Distribution Entity is fully operational expected in early 2021, AstraZeneca will invoice the Distribution Entity for its sales and marketing services provided to the Distribution Entity, and FibroGen Beijing will manufacture and supply commercial product to the Distribution Entity.

FibroGen is expected to recognize revenue based on its sales to the Distribution Entity.

Development costs will continue to be shared 50/50 between the Parties.

FibroGen, Inc. and AstraZeneca concurrently amended the US/RoW Agreement to reflect minor changes in the governance structure under the China Agreement.

We are in the process of evaluating the accounting impacts resulting from the Amendment and the establishment of the Distribution Entity, which is expected to be significant to our consolidated financial statements starting the third quarter of 2020. Among others, the accrued long-term co-promotional expenses related to the estimated amount payable to AstraZeneca for its sales and marketing efforts associated with the commercial launch and sales for roxadustat will be reduced by approximately \$82 million in the third quarter of 2020.

Additional Information Related to Collaboration Agreements

Total cash consideration received through June 30, 2020 and potential cash consideration, other than development cost reimbursement, transfer price payments, royalties and profit share, pursuant to our existing collaboration agreements are as follows:

		Cash Received Through June 30, 2020		Additional Potential Cash Payments	Total Potential Cash Payments	
	_			(in thousands)		,
Astellasrelated-party:						
Japan Agreement	\$	90,093	\$	82,500	\$	172,593
Europe Agreement		540,000		205,000		745,000
Total Astellas	·	630,093	<u> </u>	287,500		917,593
AstraZeneca:						
U.S. / RoW Agreement		439,000		810,000		1,249,000
China Agreement		77,200		299,500		376,700
Total AstraZeneca		516,200		1,109,500		1,625,700
Total revenue	\$	1,146,293	\$	1,397,000	\$	2,543,293

These collaboration agreements also provide for reimbursement of certain fully burdened research and development costs as well as direct out of pocket expenses.

RESULTS OF OPERATIONS

Revenue

		Three Months Ended June 30,		Change		Six Months Ended June 30,						
	2020	2019	\$	%	2020	2019	\$	%				
	(dollars in thousands)											
Revenue:												
License revenue	\$ —	\$ 150,581	\$ (150,581)	(100) %	\$ —	\$ 150,581	\$ (150,581)	(100) %				
Development and other revenue	18,957	40,985	(22,028)	(54) %	38,402	64,848	(26,446)	(41) %				
Product revenue, net	15,693	_	15,693	100 %	20,648	_	20,648	100 %				
Drug product revenue	8,238	_	8,238	100 %	8,238	_	8,238	100 %				
Total revenue	\$ 42,888	\$ 191,566	\$(148,678)	(78) %	\$ 67,288	\$ 215,429	\$ (148,141)	(69) %				

Our revenue to date has been generated substantially from our collaboration agreements with Astellas and AstraZeneca. In addition, we started roxadustat commercial sales in China in the third quarter of 2019.

Under our revenue recognition policy, license revenue includes amounts from upfront, non-refundable license payments and amounts allocated pursuant to the standalone selling price method from other consideration received during the periods. This revenue is generally recognized as deliverables are met and services are performed. We did not have any license revenue for the three and six months ended June 30, 2020.

Development and other revenue includes co-development and other development related services. Co-development services are recognized as revenue in the period in which they are billed to our partners, excluding China. For China co-development services, revenue is deferred until the end of the development period once all performance obligations have been satisfied. Other development related services are recognized as revenue over the noncontingent development period based on a proportional performance method. As of June 30, 2020, the future non-contingent development periods range from 12 to 60 months. Other revenues consist of sales of research and development material and have been included with development and other revenue in the consolidated statements of operations, as they have not been material for any of the periods presented.

Product revenue is recognized when our customer obtains control of promised goods or services in an amount that reflects the consideration we expect to receive in exchange for those goods or services.

Drug product revenue includes commercial-grade API sales to Astellas for purpose of roxadustat commercial launch in Japan, and is recognized when we fulfill all the delivery obligations.

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PART II—OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

We are not currently a party to any material legal proceedings.

ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below in addition to the other information included or incorporated by reference in this Quarterly Report on Form 10-Q, including our condensed consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

We have marked with an asterisk (*) those risks described below that reflect substantive changes from the risks described under Part I, Item 1A "Risk Factors" included in our Annual Report on Form 10-K for the year ended December 31, 2019.

Risks Related to Our Financial Condition and History of Operating Losses

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or sustain profitability. We may require additional financings in order to fund our operations.*

We are a biopharmaceutical company with two lead product candidates in clinical development, roxadustat in anemia in chronic kidney disease ("CKD"), myelodysplastic syndromes ("MDS"), and chemotherapy-induced anemia, and pamrevlumab in idiopathic pulmonary fibrosis ("IPF"), pancreatic cancer, Duchenne muscular dystrophy ("DMD"), and Severe Acute Respiratory Syndrome Coronavirus 2019 Disease ("COVID-19"). Most of our revenue generated to date has been based on our collaboration agreements and we have limited commercial drug product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss for the year ended December 31, 2019, 2018 and 2017 were \$77.0 million, \$86.4 million and \$120.9 million, respectively. As of June 30, 2020, we had an accumulated deficit of \$948.4 million. As of June 30, 2020, we had capital resources consisting of cash, cash equivalents and short-term investments of \$685.6 million plus \$0.2 million of long-term investments classified as available for sale securities. Despite contractual development and cost coverage commitments from our collaboration partners, AstraZeneca AB ("AstraZeneca") and Astellas Pharma Inc. ("Astellas"), and the potential to receive milestone and other payments from these partners, and despite commercialization efforts in the People's Republic of China ("China") and Japan for roxadustat for the treatment of anemia caused by CKD, we anticipate we will continue to incur losses on an annual basis for the foreseeable future. If we do not successfully develop and continue to obtain regulatory approval for our existing or any future product candidates and effectively manufacture, market and sell the product candidates that are approved, we may never achieve or sustain profitability on a quarterly or annual basis. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our failure to become and

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We believe that we will continue to expend substantial resources for the foreseeable future as we continue late-stage clinical development of roxadustat, grow our operations in China, expand our clinical development efforts on pamrevlumab, continue to seek regulatory approval, launch commercialization of our product candidates, and pursue additional indications. These expenditures will include costs associated with research and development, conducting preclinical trials and clinical trials, obtaining regulatory approvals in various jurisdictions, and manufacturing and supplying products and product candidates for ourselves and our partners. The outcome of any clinical trial and/or regulatory approval process is highly uncertain and we are unable to fully estimate the actual costs necessary to successfully complete the development and regulatory approval process for our compounds in development and any future product candidates. We believe that the net proceeds from our 2017 public offerings, our existing cash and cash equivalents, short-term and long-term investments and accounts receivable, and expected third-party collaboration revenues will allow us to fund our operating plans through at least the next 12 months. Our operating plans or third-party collaborations may change as a result of many factors, including the success of our development and commercialization efforts, operations costs (including manufacturing and regulatory), competition, and other factors that may not currently be known to us, and we therefore may need to seek additional funds sooner than planned, through offerings of public or private securities, debt financings or other sources, such as royalty monetization or other structured financings. Such financings may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. We may also seek additional capital due to favorable market conditions or strategic considerations even if we currently believe

Additional funds may not be available when we require them, or on terms that are acceptable to us. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations or activities that may be necessary to commercialize our product candidates.

Most of our recent revenue has been earned from collaboration partners for our product candidates under development.

If either or both of our Astellas and AstraZeneca collaborations were to be terminated, we could require significant additional capital in order to proceed with development and commercialization of our product candidates, including with respect to our commercialization of roxadustat for the treatment of anemia caused by CKD, or we may require additional partnering in order to help fund such development and commercialization. If adequate funds or partners are not available to us on a timely basis or on favorable terms, we may be required to delay, limit, reduce or terminate our development or commercialization efforts or other operations.

Risks Related to the Development and Commercialization of Our Product Candidates

We are substantially dependent on the success of our lead product, roxadustat, and our second compound in development, pamrevlumab.*

To date, we have invested a substantial portion of our efforts and financial resources in the research and development of roxadustat and pamrevlumab. While we have received approval of our New Drug Applications ("NDA") for roxadustat in China for CKD anemia for patients on dialysis and not on dialysis, and for roxadustat in Japan for CKD anemia in dialysis patients, we will need to make substantial additional investments in the development of roxadustat worldwide and in various indications. Our near-term prospects, including maintaining our existing collaborations with Astellas and AstraZeneca, will depend heavily on successful development and commercialization of roxadustat, including obtaining additional regulatory approvals for the commercialization of roxadustat for anemia associated with CKD.

Our other lead product candidate, pamrevlumab, is currently in clinical development for IPF, pancreatic cancer, DMD, and COVID-19. Pamrevlumab requires substantial further development and investment and we do not have a collaboration partner for support of this compound. In addition, pamrevlumab is a monoclonal antibody, which may require greater financial resources than for our small molecule, roxadustat.

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, many of which are beyond our control, and we may be unable to complete the development or commercialization of roxadustat or pamrevlumab.*

The clinical and commercial success of roxadustat and pamrevlumab will depend on a number of factors, including the following:

- the timely initiation and completion of our clinical trials, including for the duration of the COVID-19 pandemic, which could cause delays in our clinical trial initiation and patient enrollment and completion;
- our ability to demonstrate the safety and efficacy of our product candidates to the satisfaction of the relevant regulatory authorities;

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- the ultimate approval criteria (which may include non-inferiority margins and statistical analyses methods), indications, patient populations, and ultimate benefit-risk analysis used by regulatory authorities in their approval processes:
- whether we are required by the United States ("U.S.") Food and Drug Administration ("FDA") or other regulatory authorities to conduct additional clinical trials, and the scope and nature of such clinical trials, prior to approval to market our products;
- the clinical indications for which the product is approved and the labeling required by regulatory authorities for use with the product, including any warnings that may be required in the labeling;
- the receipt or timely receipt of marketing approvals from the FDA and foreign regulatory authorities, including pricing and reimbursement determinations;
- the ability to successfully commercialize, market, sell and distribute our product candidates, if approved, for marketing and sale by the FDA or foreign regulatory authorities, whether alone or in collaboration with others;
- whether we or our partners are able to recruit and retain adequate numbers of effective sales and marketing personnel for the sale of our products;
- whether we will maintain sufficient funding to cover the costs and expenses associated with creating and sustaining a capable sales and marketing organization and related commercial infrastructure;
- whether we can compete successfully as a new entrant in the treatment of anemia caused by CKD;
- our ability and the ability of our third-party manufacturing partners to manufacture quantities of our product candidates at quality levels necessary to meet regulatory requirements and at a scale sufficient to meet anticipated demand at a cost that allows us to achieve profitability;
- our success in educating health care providers, patients and the healthcare community about the benefits, risks, administration and use of our product candidates, if approved;
- acceptance of our product candidates, if approved, as safe and effective by patients and the healthcare community;
- the success of efforts to enter into relationships with large dialysis organizations involving the administration of roxadustat to dialysis patients;
- the achievement and maintenance of compliance with all regulatory requirements applicable to us and our product candidates;
- the maintenance of an acceptable benefit/risk profile of our products following any approval;
- the availability, perceived advantages, relative cost, relative safety, and relative efficacy of alternative and competitive treatments;
- the restrictions on the use of our products together with other medications, if any;
- our ability to negotiate, obtain and sustain an adequate level of pricing or reimbursement for our products by third-party payors;
- the availability of adequate coverage and reimbursement or pricing by third-party payors and government authorities;
- our ability to enforce successfully our intellectual property rights for our product candidates and against the products of potential competitors;
- our ability to avoid or succeed in third-party patent interference or patent infringement claims; and
- sufficient stability data for launch and market supply.

Many of these factors are beyond our control. Successful commercialization of our products will require significant resources and time, and there is a risk that we may not successfully commercialize them. If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our products and generate revenues, which would deprive us from additional working capital and would materially harm our ability to achieve profitability through the sale of or royalties from our product candidates.

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As a company, we have limited commercialization experience, and the time and resources to develop such experience are significant. If we fail to achieve and sustain commercial success for roxadustat, either directly or with our collaboration partners, our business would be harmed.*

We do not have a sales or marketing infrastructure and have limited experience in the sales, marketing or distribution of pharmaceutical products in any country. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales and marketing capabilities or make and maintain our existing arrangements with third parties to perform these services at a level sufficient to support our commercialization efforts.

To the extent that we would undertake sales and marketing of any of our products directly, there are risks involved with establishing our own sales, marketing and distribution capabilities. Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to effectively manage geographically dispersed sales and marketing teams;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

With respect to roxadustat, we are dependent on the commercialization capabilities of our collaboration partners, AstraZeneca and Astellas. If either such partner were to terminate its agreement with us, we would have to commercialize on our own or with another third party. We will have limited or little control over the commercialization efforts of such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products, if any, effectively. If they are not successful in commercializing our product candidates, our business and financial condition would suffer.

Commercializing roxadustat requires us to establish commercialization systems, including but not limited to, medical affairs, sales, pharmacovigilance, supply-chain, and distribution capabilities to perform our portion of the collaborative efforts. These efforts require resources and time. If we, along with Astellas and AstraZeneca, are not successful in setting our marketing, pricing and reimbursement strategy, facilitating adoption by hospitals, recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing roxadustat, which would adversely affect our business and financial condition.

Although regulatory approval has been obtained for roxadustat in China and Japan, we may be unable to obtain regulatory approval for our product candidates in other countries, or such approval may be delayed or limited, due to a number of factors, many of which are beyond our control.*

The clinical trials and the manufacturing of our product candidates are and will continue to be, and the marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the U.S. and in other countries where we intend to develop and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical trials and clinical trials that the product candidate is safe and effective for use in each indication for which approval is sought. The regulatory review and approval process is expensive and requires substantial resources and time, and in general very few product candidates that enter development receive regulatory approval. In addition, our collaboration partners for roxadustat have final control over development decisions in their respective territories and they may make decisions with respect to development or regulatory authorities that delay or limit the potential approval of roxadustat, or increase the cost of development or commercialization. Accordingly, we may be unable to successfully develop or commercialize roxadustat, pamrevlumab, or any of our other product candidates in one or more indications and jurisdictions.

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Moreover, for any Phase 3 clinical trial to support an NDA/Biologics License Application submission for approval, the FDA and foreign regulatory authorities require compliance with regulations and standards (including good clinical practices ("GCP") requirements for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials) to ensure that (1) the data and results from trials are credible and accurate; and (2) that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we as the sponsor remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable. Accordingly, the FDA or other regulatory authorities may require us to exclude the use of patient data from these unreliable clinical trials, or perform additional clinical trials before approving our marketing applications. The FDA or other regulatory authorities may even reject our application for approval or refuse to accept our future applications.

Regulatory authorities may take actions or impose requirements that delay, limit or deny approval of our product candidates for many reasons, including, among others:

- our failure to adequately demonstrate to the satisfaction of regulatory authorities that roxadustat is safe and effective in treating anemia in CKD or that pamrevlumab is safe and effective in treating IPF, pancreatic cancer, DMD or COVID-19;
- our failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- our failure of clinical trials to meet the level of statistical significance required for approval;
- the determination by regulatory authorities that additional clinical trials are necessary to demonstrate the safety and efficacy of roxadustat or pamrevlumab, or that ongoing clinical trials need to be modified in design, size, conduct or implementation;
- our product candidates may exhibit an unacceptable safety signal as they advance through clinical trials, in particular controlled Phase 3 trials:
- the clinical research organizations ("CROs") that conduct clinical trials on our behalf may take actions outside of our control that materially adversely impact our clinical trials;
- we or third-party contractors manufacturing our product candidates may not maintain current good manufacturing practices ("cGMP"), successfully pass inspection or meet other applicable manufacturing regulatory requirements;
- regulatory authorities may not agree with our interpretation of the data from our preclinical trials and clinical trials; or
- collaboration partners may not perform or complete their clinical programs in a timely manner, or at all.

Any of these factors, many of which are beyond our control, could jeopardize our or our collaboration partners' abilities to obtain regulatory approval for our product candidates in one or more indications.

The FDA or other regulatory authorities may require more information (including additional preclinical or clinical data to support approval), which may delay or prevent approval or cause us to abandon the development program altogether. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS (or other regulatory authorities may require the establishment of a similar strategy), that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us.

Preclinical, Phase 1 and Phase 2 clinical trial results may not be indicative of the results that may be obtained in larger, controlled Phase 3 clinical trials required for approval.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical and early clinical trials, which are often highly variable and use small sample sizes, may not be predictive of similar results in humans or in larger, controlled clinical trials, and successful results from clinical trials in one indication may not be replicated in other indications.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may face similar setbacks.

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We do not know whether our ongoing or planned clinical trials of roxadustat or pamrevlumab will need to be redesigned based on interim results or if we will be able to achieve sufficient patient enrollment or complete planned clinical trials on schedule.*

Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- address any physician or patient safety concerns that arise during the course of the trial;
- obtain required regulatory or institutional review board approval or guidance;
- reach timely agreement on acceptable terms with prospective CROs and clinical trial sites;
- recruit, enroll and retain patients through the completion of the trial, including for the duration of the COVID-19 pandemic;
- maintain clinical sites in compliance with clinical trial protocols;
- initiate or add a sufficient number of clinical trial sites; and
- manufacture sufficient quantities of product candidate for use in clinical trials.

In particular, identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the rate at which we can recruit and enroll patients in testing our product candidates. Patients may be unwilling to participate in clinical trials of our product candidates for a variety of reasons, some of which may be beyond our control, including:

- severity of the disease under investigation;
- availability of alternative treatments;
- size and nature of the patient population;
- eligibility criteria for and design of the study in question;
- perceived risks and benefits of the product candidate under study;
- ability to enroll patients in clinical trials during the COVID-19 pandemic;
- ongoing clinical trials of competitive agents;
- physicians' and patients' perceptions of the potential advantages of our product candidates being studied in relation to available therapies or other products under development;
- our CRO's and our trial sites' efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients and collect patient data adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate on-going or planned clinical trials.

In addition, we could encounter delays if a clinical trial is suspended or terminated by us, by the relevant institutional review boards at the sites at which such trials are being conducted, or by the FDA or other regulatory authorities. A suspension or termination of clinical trials may result from any number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or a principal investigator's determination that a serious adverse event could be related to our product candidates. Any delays in completing our clinical trials will increase the costs of the trial, delay the product candidate development and approval process and jeopardize our ability to commence marketing and generate revenues. Any of these occurrences may materially and adversely harm our business, operations, and prospects.

Our product candidates may cause or have attributed to them undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our product candidates or that may be identified as related to our product candidates by physician investigators conducting our clinical trials or even competing products in development that utilize a similar mechanism of action or act through a similar biological disease pathway could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. If we determine that there is a likely causal relationship between a serious adverse event and our product candidate, and such safety event is material or significant enough, it may result in:

- our Phase 3 clinical trial development plan becoming longer and more extensive;
- regulatory authorities increasing the data and information required to approve our product candidates and imposing other requirements; and
- our collaboration partners terminating our existing agreements.

The occurrence of any or all of these events may cause the development of our product candidates to be delayed or terminated, which could materially and adversely affect our business and prospects. Refer to "Business — Overview" in the 2019 Form 10-K for a discussion of the adverse events and serious adverse events that have emerged in clinical trials of roxadustat and pamrevlumab.

Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.

Clinical trials are conducted in representative samples of the potential patient population, which may have significant variability. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, that a more complete safety profile is identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. There have been other products, including erythropoiesis stimulating agents ("ESAs"), for which safety concerns have been uncovered following approval by regulatory authorities. Such safety concerns have led to labeling changes or withdrawal of ESAs products from the market. While our most advanced product candidate is chemically unique from ESAs, it or any of our product candidates may be subject to known or unknown risks. Patients treated with our products, if approved, may experience adverse reactions and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If safety problems occur or are identified after our product candidates reach the market, we may, or regulatory authorities may require us to amend the labeling of our products, recall our products or even withdraw approval for our products.

If we or third-party manufacturers and other service providers on which we rely cannot manufacture sufficient quantities of our products and product candidates, or at sufficient quality, or perform other services we require, we may experience delays in development, regulatory approval, launch or successful commercialization.*

Completion of our clinical trials and commercialization of our products require access to, or development of, facilities to manufacture and manage our product candidates at sufficient yields, quality and at commercial scale. Although we have entered into commercial supply agreements for the manufacture of some of our drug candidates, active pharmaceutical ingredients ("API"), intermediates or raw materials, we will need to enter into additional commercial supply agreements, including for backup or second source third-party manufacturers. We may not be able to enter into these agreements with satisfactory terms or on a timely manner.

We have limited experience manufacturing or managing third parties in manufacturing any of our product candidates in the volumes that are expected to be necessary to support large-scale clinical trials and sales. In addition, we have limited experience forecasting supply requirements or coordinating supply chain (including export management) for launch or commercialization, which is a complex process involving our third-party manufacturers and logistics providers, and for roxadustat, our collaboration partners. We may not be able to accurately forecast supplies for commercial launch, or do so in a timely manner and our efforts to establish these manufacturing and supply chain management capabilities may not meet our requirements as to quantities, scale-up, yield, cost, potency or quality in compliance with cGMP, particularly if the marketing authorization or market uptake is more rapid than anticipated or we have an unanticipated surge in demand.

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We have a limited amount of roxadustat and pamrevlumab in storage, limited capacity reserved at our third-party manufacturers, and, even if we have or are able to put supply agreements in place for our products, there are long lead times required to manufacture and scale-up the manufacture of additional supply, as required for both late-stage clinical trials, post-approval trials, and commercial supply. If we are unable to forecast, order or manufacture sufficient quantities of roxadustat or pamrevlumab on a timely basis, it may delay our development, launch or commercialization in some or all indications we are currently pursuing. Any delay or interruption in the supply of our product candidates or products could have a material adverse effect on our business and operations.

Our commercial drug product and the product we use for clinical trials must be produced under applicable cGMP regulations. Failure to comply with these regulations may require us to recall commercial product or repeat clinical trials, which would impact sales revenue or delay the regulatory approval process.

We may add or change manufacturers for our products. We may also make changes to our manufacturing processes or to our product specifications, including in order to accommodate changes in regulations, manufacturing equipment or to account for different processes at new or second source suppliers. If we make any such changes with respect to roxadustat or pamrevlumab we will need to demonstrate comparability to the products and processes already approved or in approval by various regulatory authorities, including potentially through the conduct of additional clinical trials. Even if we do demonstrate comparability, a regulatory agency could challenge that result which could delay our development or commercialization progress. Any of these occurrences may materially impact our operations and potential profitability.

We, and even an experienced third-party manufacturer, may encounter difficulties in production. Difficulties may include:

- costs and challenges associated with scale-up and attaining sufficient manufacturing yields, in particular for biologic products such as pamrevlumab, which is a monoclonal antibody;
- contracting with additional suppliers and validation/qualification of additional facilities to meet growing demand;
- supply chain issues, including coordination of multiple contractors in our supply chain and securing necessary licenses (such as export licenses);
- the timely availability and shelf life requirements of raw materials and supplies;
- equipment maintenance issues or failure;
- quality control and quality assurance issues;
- shortages of qualified personnel and capital required to manufacture large quantities of product;
- compliance with regulatory requirements that vary in each country where a product might be sold;
- capacity or forecasting limitations and scheduling availability in contracted facilities; and
- natural disasters, such as pandemics, including the COVID-19 pandemic, floods, storms, earthquakes, tsunamis, and droughts, or accidents such as fire, that affect facilities, possibly limit or postpone production, and increase costs.

The FDA and European Medicines Agency ("EMA") will do their own benefit risk analysis and may reach a different conclusion than we or our partners have internally, and these regulatory authorities may base their approval decision on different analyses, data, and statistical methods than ours

Even if we believe we have achieved positive clinical results, such as superiority or non-inferiority, in certain endpoints, populations or subpopulations, or using certain statistical methods of analysis, the FDA and EMA will each conduct their own benefit-risk analysis and may reach different conclusions, using different statistical methods, different endpoints or definitions thereof, or different patient populations or sub-populations, and regulatory authorities may change their approvability criteria based on their internal analyses and discussions with expert advisors. Regulatory authorities may approve roxadustat for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-approval clinical trials. While we will present to regulatory authorities certain pre-specified and not pre-specified sub-populations and sub-group analyses (for example, incident dialysis), multiple secondary endpoints, and multiple analytical methods (such as long-term follow up analyses), including adjusted and censored data, regulatory authorities may reject these analyses, methods, or even parts of our trial design or certain data from our studies, the rationale for our pre-specified non-inferiority margins or other portions of our statistical analysis plans. In addition, even if we are able to provide positive data with respect to certain analyses, such as incident dialysis, estimated glomerular filtration rate, hepcidin, or quality of life measures, regulatory authorities may not include such claims on any approved labeling for roxadustat, which may limit the commercialization or market opportunity for roxadustat. The failure to obtain regulatory approval, or any label, population or other approval limitations in any jurisdiction, may significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenue.

Even if we are able to obtain regulatory approval of our product candidates, the label we obtain may limit the indicated uses for which our product candidates may be marketed.

With respect to roxadustat, regulatory approvals obtained, could limit the approved indicated uses for which roxadustat may be marketed. For example, our label approved in Japan, includes the following warning: "Serious thromboembolism such as cerebral infarction, myocardial infarction, and pulmonary embolism may occur, possibly resulting in death, during treatment with roxadustat." Additionally, in the U.S., ESAs have been subject to significant safety warnings, including the "Black Box" warnings on their labels. The safety concerns relating to ESAs may result in labeling for roxadustat containing similar warnings even if our Phase 3 clinical trials do not suggest that roxadustat has similar safety issues. Even if the label for roxadustat does not contain all of the warnings contained in the "Black Box" warning for ESAs, the label for roxadustat may contain other warnings or limit the market opportunity or approved indications for roxadustat. These warnings could include warnings against exceeding specified hemoglobin targets and other warnings that derive from the lack of clarity regarding the safety issues associated with ESAs, even if our Phase 3 clinical trials do not themselves raise safety concerns.

We face substantial competition, which may result in others discovering, developing or commercializing products before, or more successfully, than we do.*

The development and commercialization of new pharmaceutical products is highly competitive. Our future success depends on our ability and/or the ability of our collaboration partners to achieve and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to discover, develop and commercialize new products with superior efficacy, convenience, tolerability, and safety. We expect that in many cases, the products that we commercialize will compete with existing, market-leading products of companies that have large, established commercial organizations.

If roxadustat is approved and launched commercially, competing drugs are expected to include ESAs, particularly in those patient segments where ESAs are used. Currently available ESAs include epoetin alfa (EPOGEN ®, marketed by Amgen Inc. in the U.S., Procrit ® and Erypo ®/Eprex ®, marketed by Johnson & Johnson Inc., and Espo ® marketed by Kyowa Hakko Kirin in Japan and China), darbepoetin (Amgen/Kyowa Hakko Kirin's Aranesp ® and NESP ®) and Mircera ® marketed by Hoffmann-La Roche ("Roche") outside of the U.S. and by Vifor Pharma, a Roche licensee, in the U.S. and Puerto Rico, as well as biosimilar versions of these currently marketed ESA products. ESAs have been used in the treatment of anemia in CKD for more than 30 years, serving a significant majority of dialysis CKD patients. While non-dialysis CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated, some non-dialysis patients under nephrology care may be receiving ESA therapy. It may be difficult to encourage healthcare providers and patients to switch to roxadustat from products with which they have become familiar.

We may also face competition from potential new anemia therapies currently in clinical development, including in those patient segments not currently addressed by ESAs. Companies that are currently developing hypoxia-inducible factor ("HIF") prolyl hydroxylase ("HIF-PH") inhibitors for anemia in CKD indications include GlaxoSmithKline plc ("GSK"), Bayer Corporation ("Bayer"), Akebia Therapeutics, Inc. ("Akebia"), Japan Tobacco, and Zydus Cadila. Akebia is currently conducting Phase 3 studies in CKD patients on dialysis and not on dialysis, as well as a Phase 2 study evaluating pharmacokinetics and pharmacodynamics in dialysis patients with three-times weekly versus once-a-day dosing. In Japan, Mitsubishi Tanabe Pharmaceutical Corporation, Akebia's collaboration partner, received approval for vadadustat on June 29, 2020 for the treatment of anemia of CKD patients on and not on dialysis. Price listing for and subsequent launch of vadadustat in Japan is expected in Q3 2020. GSK is also conducting global Phase 3 studies in CKD patients on dialysis and not on dialysis, and expects to complete those studies by March 2022. GSK and Kyowa Hakko Kirin announced in November 2018 that the two companies signed a strategic commercialization deal in Japan for daprodustat. GSK received approval for daprodustat in Japan on June 29, 2020 for the treatment of anemia of CKD patients on and not on dialysis. Price listing for and subsequent launch of daprodustat in Japan is expected in Q3 2020. Bayer has completed global Phase 2 studies and its HIF-PH inhibitor is now in Phase 3 development in CKD populations on dialysis and not on dialysis in Japan. Japan Tobacco submitted an NDA for treatment of anemia associated with CKD in Japan in November 2019, supported by the six Phase 3 studies conducted in CKD patients on dialysis and not on dialysis in Japan, and its partner JW Pharmaceuticals started a Phase 3 study in dialysis patients in Korea in 2019. Zydus Cadila (India) started Phase 3 studies in dialysis and non-dialysis CKD patients in India in 2019. In July 2020, Zydus received approval from the FDA to begin studies of desidustat for the treatment of chemotherapy-induced anemia, which could potentially be competitive with roxadustat within this indication.

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In addition, there are other companies developing or that have developed biologic therapies for the treatment of other anemia indications that we may also seek to pursue in the future, including anemia of MDS. For example, Acceleron Pharma, Inc., in partnership with Celgene Corporation, a Bristol-Myers Squibb company ("Celgene"), developed Reblozyl® (luspatercept), a protein therapeutic. Reblozyl was approved for treatment of anemia in adult patients with \(\beta\)-thalassemia in November 2019, and in April 2020 for treatment of anemia failing an ESA therapy and requiring two or more red blood cell transfusions over eight weeks in adult patients with very low- to intermediate-risk MDS with ring sideroblast or with myelodysplastic or myeloproliferative neoplasm with ring sideroblasts and thrombocytosis. In June 2020, Acceleron received European Commission approval for luspatercept for the treatment of transfusion-dependent anemia in adult patients with MDS or \(\beta\)-thalassemia. In Japan, Celgene started a luspatercept Phase 2 study in May 2019. We may face competition for patient recruitment, enrollment for clinical trials, and potentially in commercial sales. There may also be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat if and when it is commercialized.

In China, locally manufactured epoetin alfa are offered by Chinese pharmaceutical companies such as EPIAO marketed by 3SBio Inc. as well as more than 15 other local manufacturers. We may also face competition by HIF-PH inhibitors from other companies such as Akebia, Bayer, and GSK, which was authorized by the National Medical Products Administration ("NMPA") to conduct trials in China to support its ex-China regulatory filings. Two domestic companies, Jiangsu Hengrui Medicine Co., Ltd. and Guandong Sunshine Health Investment Co., Ltd, have been permitted by the NMPA to conduct clinical trials for CKD anemia patients both on dialysis and not on dialysis, and 3SBio Inc. has submitted a clinical trial application to the NMPA to initiate trials for their HIF-PH inhibitor. Another domestic company, China Medical System, in-licensed desidustat, a compound that is currently in Phase 3 trials in India, from Zydus Cadila for greater China in January 2020. Akebia announced in December 2015 that it had entered into a development and commercialization partnership with Mitsubishi Tanabe Pharmaceutical Corporation for its HIF-PH inhibitor vadadustat in Japan, Taiwan, South Korea, India and certain other countries in Asia, and announced in April 2017 an expansion of their U.S. collaboration with Otsuka to add markets, including China. 3SBio Inc. announced in 2016 its plan to begin a Phase 1 clinical trial of a HIF-PH inhibitor for the China market.

The first biosimilar ESA, Pfizer's Retacrit® (epoetin zeta), entered the U.S. market in November 2018. Market penetration of Retacrit and the potential addition of other biosimilar ESAs currently under development may alter the competitive and pricing landscape of anemia therapy in CKD patients on dialysis under the end-stage renal disease bundle. The patents for Amgen's EPOGEN® (epoetin alfa) expired in 2004 in Europe, and the final material patents in the U.S. expired in May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in Europe, China and other territories. In the U.S., a few ESA biosimilars are currently under development. Sandoz, a division of Novartis, markets Binocrit® (epoetin alfa) in Europe and may file a biosimilar Biologics License Application in the U.S.

The majority of the current CKD anemia market focuses on dialysis patients, who visit dialysis centers on a regular basis, typically three times a week, and anemia therapies are administered as part of the visit. Two of the largest operators of dialysis clinics in the U.S., DaVita Healthcare Partners Inc. ("DaVita"), and Fresenius Medical Care AG & Co. KGaA ("Fresenius"), collectively provide dialysis care to more than 80% of U.S. dialysis patients, and therefore have historically executed long-term contracts including rebate terms with Amgen. DaVita has a six-year sourcing and supply agreement with Amgen effective through 2022. Fresenius' contract with Amgen expired in 2015, following which Fresenius is providing Roche's ESA Mircera® to a significant portion of its U.S. dialysis patients. Successful penetration in this market will likely require a definitive agreement with Fresenius and/or DaVita, on favorable terms and on a timely basis.

If approved and launched commercially to treat IPF, pamrevlumab is expected to compete with Roche's Esbriet® (pirfenidone), and Boehringer Ingelheim's Ofev® (nintedanib). We believe that if pamrevlumab can be shown to safely stabilize or reverse lung fibrosis, and thus stabilize or improve lung function in IPF patients, it can compete with pirfenidone and nintedanib for market share in IPF. However, it may be difficult to encourage treatment providers and patients to switch to pamrevlumab from an oral product with which they are already familiar to a product delivered via in-office infusion. Furthermore, pirfenidone and nintedanib may be produced as generics in the near future. We may also face competition from potential new IPF therapies in recruitment and enrollment in our clinical trials and potentially in commercialization.

Pamrevlumab is a monoclonal antibody which may be more expensive and less convenient than oral small molecules such as nintedanib and pirfenidone. Other potential competitive product candidates in various stages of development for IPF include Galapagos NV's GLPG1690 and GLPG1205, Kadmon Holdings, Inc.'s KD025, Liminal BioSciences' PBI-4050, and Roche/Promedior, Inc.'s PRM-151. In particular, GLPG1690 is in a Phase 3 program consisting of two clinical trials with 750 subjects each, intended to support both the U.S. NDA and Marketing Authorization Application ("MAA") in Europe.

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If pamrevlumab is approved and launched commercially to treat locally advanced pancreatic cancer patients who are not candidates for surgical resection, pamrevlumab may face competition from products currently used for pancreatic cancer. These include FOLFRINOX, a combination chemotherapy regimen of folic acid, 5-fluouracil, oxaliplatin and irinotecan, and agents seeking approval in combination with gemcitibine and nab-paclitaxel from companies such as Rafael Pharma's defactinib/CPI-613 and Merrimack's istiratumab. Gemcitabine and/or nab-paclitaxel are the current standard of care in the first-line treatment of metastatic pancreatic cancer.

Celgene Corporation's Abraxane® (nab-paclitaxel) was launched in the U.S. and Europe in 2013 and 2014, and was the first drug approved in this disease in nearly a decade.

If approved and launched commercially to treat DMD, pamrevlumab is expected to face competition from drugs that have been approved in major markets such as the U.S., EU, and Japan. On September 19, 2016, the FDA approved Sarepta Therapeutics Inc.'s ("Sarepta") Exondys 51^{TM} (eteplirsen). This was the first drug approved to treat DMD. Exondys 51 is approved to treat patients who have a mutation of the dystrophin gene amenable to exon 51 skipping, representing approximately 13% of patients with DMD. In Europe, Sarepta received a negative opinion for its marketing application for eteplirsen from the EMA in September 2018. Sarepta has reported a full year Exondys 51 revenue of \$380 million in 2019. Sarepta's Vyondys 53^{TM} (golodirsen) was also approved by the FDA in December 2019 for patients with a confirmed genetic mutation that is amenable to exon 53 skipping, which accounts for 8% of the DMD population.

PTC Therapeutics' product Translarna TM received a conditional approval in Europe in 2014, which was renewed in November 2016 with a request for a new randomized placebo-controlled 18-month study by the Committee for Medicinal Products for Human Use of the EMA; however, the FDA informed the sponsor in a complete response letter in October 2017, as well as in its response to PTC Therapeutics' appeal, that the FDA is unable to approve the application in its current form. An additional Phase 3 study is currently ongoing. While Translarna TM targets a different set of DMD patients from those targeted by Sarepta's Exondys 51®, it is also limited to a subset of patients who carry a specific mutation. Conversely, pamrevlumab is intended to treat DMD patients without limitation to type of mutation.

Pamrevlumab may also face competition from other drugs currently in clinical development in patient recruiting and enrollment in clinical trials, and, if approved, in commercialization. Examples of those compounds currently under clinical development are the drug candidates from Pfizer, Catabasis Pharmaceuticals ("Catabasis"), Santhera Pharmaceuticals ("Santhera") and Sarepta. Pfizer initiated a Phase 3 study with PF-06939926, its AAV9 minidystrophin gene therapy for DMD in February 2020. Catabasis' edasalonexent was reported to have preserved muscle function and slowed the progression of DMD compared to rates of change in the control period prior to treatment with edasalonexent in a Phase 2 study, and is currently undergoing Phase 3 development. Santhera's Puldysa® (idebenone) MAA for treatment of DMD was filed with the EMA in May 2019, and the opinion from the Committee for Medicinal Products for Human Use is expected in the third quarter of 2020. The FDA requested additional clinical data from the idebenone Phase 3 trial currently ongoing in the U.S. and Europe. Santhera offers compassionate use of idebenone in patients with DMD in U.S. and UK. Sarepta's SRP-9001 is an investigational gene therapy for DMD. Sarepta announced in December 2019 the licensing agreement with Roche that grants Roche the commercial rights to SRP-9001 outside the U.S.

The success of any or all of these potential competitive products may negatively impact the development and potential for success of pamrevlumab. In addition, any competitive products that are on the market or in development may compete with pamrevlumab for patient recruitment and enrollment for clinical trials or may force us to change our clinical trial design, including, in order to compare pamrevlumab against another drug, which may be the new standard of care.

Moreover, many of our competitors have significantly greater resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients, manufacturing pharmaceutical products, and commercialization. In the potential anemia market for roxadustat, for example, large and established companies such as Amgen and Roche, among others, compete aggressively to maintain their market shares. In particular, the currently marketed ESA products are supported by large pharmaceutical companies that have greater experience and expertise in commercialization in the anemia market, including in securing reimbursement, government contracts and relationships with key opinion leaders; conducting testing and clinical trials; obtaining and maintaining regulatory approvals and distribution relationships to market products; and marketing approved products. These companies also have significantly greater scale, research and marketing capabilities than we do and may also have products that have been approved or are in later stages of development and have collaboration agreements in our target markets with leading dialysis companies and research institutions. If we and our collaboration partners are not able to compete effectively against existing and potential competitors, our business and financial condition may be materially and adversely affected.

No or limited reimbursement or insurance coverage of our approved products, if any, by third-party payors may render our products less attractive to patients and healthcare providers.

Market acceptance and sales of any approved products will depend significantly on reimbursement or coverage of our products by government or third-party payors and may be affected by existing and future healthcare reform measures or prices of related products for which the government or third-party reimbursement applies. Coverage and reimbursement by the government or a third-party payor may depend upon a number of factors, including the payor's determination that use of a product is:

- a covered benefit under applicable health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor, which we may not be able to provide. Furthermore, the reimbursement policies of third-party payors may significantly change in a manner that renders our clinical data insufficient for adequate reimbursement or otherwise limits the successful marketing of our products. Even if we obtain coverage for our product candidates, third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. For example, the initial roxadustat reimbursement prices set by the Ministry of Health, Labour and Welfare in Japan in November 2019 did not reflect innovation premium over the current ESA therapy, despite roxadustat's advantages observed in our clinical programs. We believe the Japanese authority's decision was primarily based on the comparability of roxadustat shown in the Japan Phase 3 studies that supported the Japan NDA, that was not designed to evaluate the outcome and additional efficacy and safety data observed in the large global Phase 3 programs that included over 8,000 patients. We have no control over whether the agency will revisit the pricing once they review the comprehensive data from the global Phase 3 program including the major adverse cardiac event /MACE plus hospitalized unstable angina and hospitalized congestive heart failure outcomes. If reimbursement is not available or is available only to limited levels or only in subsets of the dialysis and non-dialysis populations, we may not be able to successfully commercialize certain of our products, or in particular jurisdictions.

Price controls may limit the price at which products such as roxadustat, if approved, are sold. For example, reference pricing is used by various Europe member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or our partner may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unacceptable levels, we or our partner may elect not to commercialize our products in such countries, and our business and financial condition could be adversely affected.

Risks Related to COVID-19

Our business could be adversely affected by the ongoing COVID-19 global pandemic as a result of the current and potential future impacts on our commercialization efforts, supply chain, regulatory and clinical development activities, and other business operations, in addition to the impact of a global economic slowdown.*

Our business could be adversely affected by the effects of the COVID-19 pandemic, which has resulted in various and evolving government-mandated restrictions in order to reduce the spread of the disease.

The effects of the COVID-19 pandemic, the associated government-mandated restrictions and the other effects on healthcare systems, the economy, and society as a whole, may negatively impact productivity, disrupt our business, and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the progression of the disease, the length and severity of the restrictions, and other impacts and limitations on our ability to conduct our business in the ordinary course. These disruptions in our operations could negatively impact our business, operating results, and financial condition. The extent of the impact on the COVID-19 pandemic on our business and financial results will continue to depend on numerous evolving factors that we are not able to accurately predict and which will vary by market, including the duration and scope of the pandemic, global economic conditions during and after the pandemic, and governmental actions that have been taken, or may be taken in the future, in response to the pandemic.

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We have taken measures to minimize the health risks of COVID-19 to our staff, patients, healthcare providers, and their communities, as their safety and well-being are our top priority. Despite these efforts, there is a risk that one or more of our employees, including members of senior management, could contract COVID-19. Certain jurisdictions have begun re-opening only to return to restrictions in the face of increases in new COVID-19 cases. Our U.S. employees are working remotely when possible, and we may experience reduced productivity due to the remote work environment. In addition, there are other risks from remote work including but not limited to the potential for reduced oversight of third parties we work with, such as manufacturing and clinical sites. In China, our staff have returned to work in our offices, manufacturing plants, and are performing medical affairs out in the field.

Most of our, and our partners', commercial launch activities are continuing, and have resumed in China after the government shutdown during February and March. However, sales growth of roxadustat may be slowed due to continued social distancing measures, behaviors, or other restrictions. If there are any further COVID-19 outbreaks, we or our partners may need to re-institute or tighten restrictions on our operations.

While our clinical trials for MDS, CIA and locally advanced pancreatic cancer have continued to enroll, enrollment for IPF was paused at the beginning of the second quarter and has since resumed. However, we have seen impacts from COVID-19 on all of our clinical trials to varying degrees. There is a risk that any or all of our clinical trials will be delayed due to slowed or paused enrollment or site initiation, and direct COVID-19 impacts to clinical sites and clinical service providers. In addition, while we are trying to mitigate the effect of COVID-19 on existing patients, it is possible that some patients may not be able to continue to comply with protocols, which could further delay our clinical trial progress.

We believe we have sufficient roxadustat and pamrevlumab supplies for our expected commercial and clinical requirements over the next year and we and our manufacturing partners are currently continuing manufacturing operations. However, we only have a limited stockpile of these drug supply products, and therefore, if there is a greater impact from the COVID-19 pandemic than we have expected, or if manufacturing operations are halted again, we could face shortages in our global supply chains.

Any such supply disruptions could adversely impact our clinical development and ability to generate revenues from our approved products and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

Due to these and potentially additional business disruptions, there may be delays to any of our business areas including our drug supply chains, problems with our distribution or warehousing vendors, or delays to our (and our partners') clinical trials or other development efforts, or commercialization and launch activities. The full extent of these effects are unknown, but all of them could have a material impact on our operations and revenue.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this "*Risk Factors*" section.

Risks Related to Our Reliance on Third Parties

If our collaborations with Astellas or AstraZeneca were terminated, if Astellas or AstraZeneca were to prioritize other initiatives over their collaborations with us, whether as a result of a change of control or otherwise, if conflicts arise between us and Astellas or AstraZeneca, or if Astellas or AstraZeneca becomes our competitor in the future, our ability to successfully develop and commercialize our product candidates would suffer.*

We have entered into collaboration agreements with respect to the development and commercialization of our lead product candidate, roxadustat, with Astellas and AstraZeneca. These agreements provide for reimbursement of our development costs by our collaboration partners and also provide for commercialization of roxadustat throughout the major territories of the world.

Our agreements with Astellas and AstraZeneca provide each of them with the right to terminate their respective agreements with us, upon the occurrence of negative clinical results, delays in the development and commercialization of our product candidates or adverse regulatory requirements or guidance. The termination of any of our collaboration agreements would require us to fund and perform the further development and commercialization of roxadustat in the affected territory, or pursue another collaboration, which we may be unable to do, either of which could have an adverse effect on our business and operations. In addition, each of those agreements provides our respective partners the right to terminate any of those agreements upon written notice for convenience. Moreover, if Astellas or AstraZeneca, or any successor entity, were to determine that their collaborations with us are no longer a strategic priority, or if either of them or a successor were to reduce their level of commitment to their collaborations with us, our ability to develop and commercialize roxadustat could suffer. In addition, some of our collaborations are exclusive and preclude us from entering into additional collaboration agreements with other parties in the area or field of exclusivity.

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If we fail to establish and maintain strategic collaborations related to our product candidates, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise at significant cost. This in turn may negatively affect the development of our other product candidates as we direct resources to our most advanced product candidates.

Our collaboration partners also have certain rights to control decisions regarding the development and commercialization of our product candidates with respect to which they are providing funding. If we have a disagreement over strategy and activities with our collaboration partners, our plans for obtaining approval may be revised and negatively affect the anticipated timing and potential for success of our product candidates. Even if a product under a collaboration agreement is approved, we will remain substantially dependent on the commercialization strategy and efforts of our collaboration partners, and neither of our collaboration partners has experience in commercialization of an anemia drug, or novel drug such as roxadustat in the dialysis market. If our collaboration partners are unsuccessful in their commercialization efforts, our results will be affected.

With respect to our collaboration agreements for roxadustat, there are additional complexities in that we and our collaboration partners, Astellas and AstraZeneca, must reach consensus on our development programs and regulatory activities, including for the NDA in the U.S. and the MAA in Europe. Multi-party decision-making is complex and involves significant time and effort, and there can be no assurance that the parties will cooperate or reach consensus, or that one or both of our partners will not ask to proceed independently in some or all of their respective territories or functional areas of responsibility in which the applicable collaboration partner would otherwise be obligated to cooperate with us. Any disputes or lack of cooperation with us by either Astellas or AstraZeneca may negatively impact the timing or success of our regulatory approval applications.

We intend to conduct proprietary research programs in specific disease areas that are not covered by our collaboration agreements. Our pursuit of such opportunities could, however, result in conflicts with our collaboration partners in the event that any of our collaboration partners takes the position that our internal activities overlap with those areas that are exclusive to our collaboration agreements. Moreover, disagreements with our collaboration partners could develop over rights to our intellectual property, including the enforcement of those rights. In addition, our collaboration agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaboration partners could lead to the termination of our collaboration agreements, delay collaborative activities, reduce our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaboration partners, and could impact our commercial results.

Certain of our collaboration partners could also become our competitors in the future. If our collaboration partners develop competing products, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our product candidates, the development and commercialization of our product candidates and products could be delayed.

We rely on third parties for the conduct of most of our preclinical and clinical trials for our product candidates, and if our third-party contractors do not properly and successfully perform their obligations under our agreements with them, we may not be able to obtain or may be delayed in receiving regulatory approvals for our product candidates.*

We rely heavily on university, hospital, dialysis centers and other institutions and third parties, including the principal investigators and their staff, to carry out our clinical trials in accordance with our clinical protocols and designs. We also rely on a number of third-party CROs to assist in undertaking, managing, monitoring and executing our ongoing clinical trials, including those for roxadustat. We expect to continue to rely on CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our development efforts in the future, including our continued development of roxadustat. We compete with many other companies for the resources of these third parties, and large pharmaceutical companies often have significantly more extensive agreements and relationships with such third-party providers, and such third-party providers may prioritize the requirements of such large pharmaceutical companies over ours. The third parties on whom we rely may terminate their engagements with us at any time, which may cause delay in the development and commercialization of our product candidates. If any such third party terminates its engagement with us or fails to perform as agreed, we may be required to enter into alternative arrangements, which would result in significant cost and delay to our product development program. Moreover, our agreements with such third parties generally do not provide assurances regarding employee turnover and availability, which may cause interruptions in the research on our product candidates by such third parties.

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Moreover, while our reliance on these third parties for certain development and management activities will reduce our control over these activities, it will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP requirements for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results from trials are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we, as the sponsor, remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites.

If any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, other regulations, trial protocol or other requirements under their agreements with us, the quality or accuracy of the data they obtain may be compromised or unreliable, and the trials of our product candidates may not meet regulatory requirements. If trials do not meet regulatory requirements or if these third parties need to be replaced, the development of our product candidates may be delayed, suspended or terminated, regulatory authorities may require us to exclude the use of patient data from our approval applications or perform additional clinical trials before approving our marketing applications. Regulatory authorities may even reject our application for approval or refuse to accept our future applications for an extended time period. We cannot assure that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements or that our results may be used in support of our regulatory submissions. If any of these events occur, we may not be able to obtain regulatory approval for our product candidates on a timely basis, at a reasonable cost, or at all.

We currently rely, and expect to continue to rely, on third parties to conduct many aspects of our product manufacturing and distribution, and these third parties may not perform satisfactorily.*

We do not have operating manufacturing facilities at this time other than our roxadustat manufacturing facility in China, and our current commercial manufacturing facility plans in China are not expected to satisfy the requirements necessary to support development and commercialization outside of China. Other than in and for China specifically, we do not expect to independently manufacture our products. We currently rely, and expect to continue to rely, on third parties to scale-up, manufacture and supply roxadustat and our other product candidates outside of China. We also rely entirely on third parties for distribution in China. Risks arising from our reliance on third-party manufacturers include:

- reduced control and additional burdens of oversight as a result of using third-party manufacturers and distributors for all aspects of manufacturing activities, including regulatory compliance and quality control and quality assurance;
- termination of manufacturing agreements, termination fees associated with such termination, or nonrenewal of manufacturing agreements with third parties may negatively impact our planned development and commercialization activities;
- the possible misappropriation of our proprietary technology, including our trade secrets and know-how; and
- disruptions to the operations of our third-party manufacturers, distributors or suppliers unrelated to our product, including the merger, acquisition, or bankruptcy of a manufacturer or supplier or a catastrophic event, including disruption resulting from the COVID-19 pandemic, affecting our manufacturers, distributors or suppliers.

Any of these events could lead to development delays or failure to obtain regulatory approval or affect our ability to successfully commercialize our product candidates. Some of these events could be the basis for action by the FDA or another regulatory authority, including injunction, recall, seizure or total or partial suspension of production.

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The facilities used by our contract manufacturers to manufacture our product candidates must pass inspections by the FDA and other regulatory authorities. Although, except for China, we do not control the manufacturing operations of, and expect to remain completely dependent on, our contract manufacturers for manufacture of drug substance and finished drug product, we are ultimately responsible for ensuring that our product candidates are manufactured in compliance with cGMP requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our or our collaboration partners' specifications, or the regulatory requirements of the FDA or other regulatory authorities, we may not be able to secure and/or maintain regulatory approval for our product candidates and our development or commercialization plans may be delayed. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. In addition, although our longer-term agreements are expected to provide for requirements to meet our quantity and quality requirements to manufacture our products candidates for clinical studies and commercial sale, we will have minimal direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel and we expect to rely on our audit rights to ensure that those qualifications are maintained to meet our requirements. If our contract manufacturers' facilities do not pass inspection by regulatory authorities, or if regulatory authorities do not approve these facilities for the manufacture of our products, or withdraw any such approval in the future, we would need to identify and qualify alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products, if approved. Moreover, any failure of our thirdparty manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or adverse regulatory consequences, including clinical holds, warnings or untitled letters, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which would be expected to significantly and adversely affect supplies of our products to us and our collaboration partners.

Other than for Catalent, our commercial third-party supplier of roxadustat drug product in the U.S. and Europe, most of our other third-party manufacturers may terminate their engagement with us at any time and we have not yet entered into any commercial supply agreements for the manufacture of drug substance, API, or drug products. With respect to roxadustat, AstraZeneca and Astellas have certain rights to assume manufacturing of roxadustat and the existence of those rights may limit our ability to enter into favorable long-term supply agreements, if at all, with other third-party manufacturers. In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access and prioritization to manufacture. Certain third-party manufacturers may be contractually prohibited from manufacturing our product due to non-compete agreements with our competitors or a commitment to grant another party priority relative to our products. There are a limited number of third-party manufacturers that operate under cGMP and that might be capable of manufacturing to meet our requirements. Due to the limited number of third-party manufacturers with the contractual freedom, expertise, required regulatory approvals and facilities to manufacture our products on a commercial scale, identifying and qualifying a replacement third-party manufacturer would be expensive and time-consuming and may cause delay or interruptions in the production of our product candidates or products, which in turn may delay, prevent or impair our development and commercialization efforts.

We have a letter agreement with IRIX Pharmaceuticals, Inc. ("IRIX"), a third-party manufacturer that we have used in the past, pursuant to which we agreed to negotiate a single source manufacturing agreement that included a right of first negotiation for the cGMP manufacture of HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third-party bids within 5%. The exclusive right to manufacture extends for five years after approval of an NDA for those compounds, and any agreement would provide that no minimum amounts would be specified until appropriate by forecast and that we and a commercialization partner would have the rights to contract with independent third parties that exceed IRIX's internal manufacturing capabilities or in the event that we or our commercialization partner determines for reasons of continuity of supply and security that such a need exists, provided that IRIX would supply no less than 65% of the product if it is able to provide this level of supply. Subsequent to the letter agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the letter agreement with respect to the single source manufacturing agreement, and if we were to enter into any such exclusive manufacturing agreement, there can be no assurance that IRIX will not assert a claim for right to manufacture roxadustat or that IRIX could manufacture roxadustat successfully and in accordance with applicable regulations for a commercial product and the specifications of our collaboration partners. In 2015, Patheon Pharmaceuticals Inc., a business unit of DPx Holdings B.V. ("Patheon"), acquired IRIX, and in 2017, ThermoFisher Scientific Inc. acquired Patheon.

If any third-party manufacturer terminates its engagement with us or fails to perform as agreed, we may be required to find replacement manufacturers, which would result in significant cost and delay to our development programs. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such third party or potential second source manufacturer. In any event, with any third-party manufacturer we expect to enter into technical transfer agreements and share our know-how with the third-party manufacturer, which can be time-consuming and may result in delays. These delays could result in a suspension or delay of marketing roxadustat.

Certain of the components of our product candidates are acquired from single-source suppliers and have been purchased without long-term supply agreements. The loss of any of these suppliers, or their failure to supply us with supplies of sufficient quantity and quality to complete our drug substance or finished drug product of acceptable quality and an acceptable price, would materially and adversely affect our business.

We do not have an alternative supplier of certain components of our product candidates. We may be unable to enter into long-term commercial supply arrangements for some of our products, or do so on commercially reasonable terms, which could have a material adverse impact upon our business. In addition, we currently rely on our contract manufacturers to purchase from third-party suppliers some of the materials necessary to produce our product candidates. We do not have direct control over the acquisition of those materials by our contract manufacturers.

The logistics of our supply chain, which include shipment of materials and intermediates from countries such as China and India add additional time and risk (including risk of loss) to the manufacture of our product candidates. While we have in the past maintained sufficient inventory of materials, API, and drug product to meet our and our collaboration partners' needs for roxadustat to date, the lead-time and regulatory approvals required to source from and into countries outside of the U.S. increase the risk of delay and potential shortages of supply.

Risks Related to Our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.*

We rely upon a combination of patents, trade secret protection, and contractual arrangements to protect the intellectual property related to our technologies. We will only be able to protect our products and proprietary information and technology by preventing unauthorized use by third parties to the extent that our patents, trade secrets, and contractual position allow us to do so. Any disclosure to or misappropriation by third parties of our trade secrets or confidential information could compromise our competitive position. Moreover, we are involved in, have in the past been involved in, and may in the future be involved in legal or administrative proceedings involving our intellectual property initiated by third parties, and which proceedings can result in significant costs and commitment of management time and attention. As our product candidates continue in development, third parties may attempt to challenge the validity and enforceability of our patents and proprietary information and technologies.

We also are involved in, have in the past been involved in, and may in the future be involved in initiating legal or administrative proceedings involving the product candidates and intellectual property of our competitors. These proceedings can result in significant costs and commitment of management time and attention, and there can be no assurance that our efforts would be successful in preventing or limiting the ability of our competitors to market competing products.

Composition-of-matter patents relating to the API are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection not limited to any one method of use. Method-of-use patents protect the use of a product for the specified method(s), and do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. We rely on a combination of these and other types of patents to protect our product candidates, and there can be no assurance that our intellectual property will create and sustain the competitive position of our product candidates.

Biotechnology and pharmaceutical product patents involve highly complex legal and scientific questions and can be uncertain. Any patent applications that we own or license may fail to result in issued patents. Even if patents do successfully issue from our applications, third parties may challenge their validity or enforceability, which may result in such patents being narrowed, invalidated, or held unenforceable. Even if our patents and patent applications are not challenged by third parties, those patents and patent applications may not prevent others from designing around our claims and may not otherwise adequately protect our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, competitors with significantly greater resources could threaten our ability to commercialize our product candidates. Discoveries are generally published in the scientific literature well after their actual development, and patent applications in the U.S. and other countries are typically not published until 18 months after their filing, and in some cases are never published. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or patent applications, or that we or our licensors were the first to file for patent protection covering such inventions. Subject to meeting other requirements for patentability, for U.S. patent applications filed prior to March 16, 2013, the first to invent the claimed invention is entitled to receive patent protection for that invention while, outside the U.S., the first to file a patent application encompassing the invention is entitled to patent protection for the invention. The U.S. moved to a "first to file" system under the Leahy-Smith America Invents Act, effective March 16, 2013. This system also includes procedures for challenging issued patents and pending patent applications, which creates additional uncertainty. We may become involved in opposition or interference proceedings challenging our patents and patent applications or the patents and patent applications of others, and the outcome of any such proceedings are highly uncertain. An unfavorable outcome in any such proceedings could reduce the scope of or invalidate our patent rights, allow third parties to commercialize our technology and compete directly with us, or result in our inability to manufacture, develop or commercialize our product candidates without infringing the patent rights of others.

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In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to acknowledge ownership by FibroGen of inventions conceived as a result of employment from the point of conception and, to the extent necessary, perfect such ownership by assignment, and we require all of our employees, consultants, advisors and any third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how and other information and technology. Furthermore, the laws of some foreign countries, in particular, China, where we have operations, do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business and operations.

Intellectual property disputes with third parties and competitors may be costly and time consuming, and may negatively affect our competitive position.*

Our commercial success may depend on our avoiding infringement of the patents and other proprietary rights of third parties as well as on enforcing our patents and other proprietary rights against third parties. Pharmaceutical and biotechnology intellectual property disputes are characterized by complex, lengthy and expensive litigation over patents and other intellectual property rights. We may initiate or become party to or be threatened with future litigation or other proceedings regarding intellectual property rights with respect to our product candidates and competing products.

As our product candidates progress toward commercialization, we or our collaboration partners may be subject to patent infringement claims from third parties. We attempt to ensure that our product candidates do not infringe third-party patents and other proprietary rights. However, the patent landscape in competitive product areas is highly complex, and there may be patents of third parties of which we are unaware that may result in claims of infringement. Accordingly, there can be no assurance that our product candidates do not infringe proprietary rights of third parties, and parties making claims against us may seek and obtain injunctive or other equitable relief, which could potentially block further efforts to develop and commercialize our product candidates including roxadustat or pamrevlumab. Any litigation involving defense against claims of infringement, regardless of the merit of such claims, would involve substantial litigation expense and would be a substantial diversion of management time.

We may consider administrative proceedings and other means for challenging third-party patents and patent applications. An unfavorable outcome in any such challenge could require us to cease using the related technology and to attempt to license rights to it from the prevailing third party, which may not be available on commercially reasonable terms, if at all, in which case our business could be harmed.

We intend, if necessary, to vigorously enforce our intellectual property in order to protect the proprietary position of our product candidates, including roxadustat and pamrevlumab. In addition, our collaboration partners who have been granted licenses to our patents may also have rights related to enforcement of those patents. Active efforts to enforce our patents by us or by our partners may include litigation, administrative proceedings, or both, depending on the potential benefits that might be available from those actions and the costs associated with undertaking those efforts against third parties. We carefully review and monitor publicly available information regarding products that may be competitive with our product candidates and assert our intellectual property rights where appropriate.

Third parties may also challenge our patents and patent applications, through interference, reexamination, *inter partes* review, and post-grant review proceedings before the U.S. Patent and Trademark Office ("USPTO") or through comparable proceedings in other territories. For example, various administrative and court challenges have been filed in several territories including the U.S., Europe, the U.K., Canada, and Japan, against our HIF anemia-related technologies patent portfolio. In the U.S., we have previously prevailed in administrative challenges to various patents in in this portfolio that are owned or exclusively licensed by FibroGen, maintaining our intellectual property in all relevant scope.

On April 20, 2020, in response to an invalidation action brought against certain FibroGen UK patents by Akebia, the UK court handed down a decision invalidating UK designations of European Patent Nos. 1463823, 1633333, 2298301, 2322153, and 2322155. The UK designation to European Patent No. 2289531 was held to be valid in amended form, but not infringed by Akebia. We and our partner Astellas have filed an appeal of the decision in the UK Court of Appeal. We note that narrowing or even revocation of any of the HIF anemia-related technology patents does not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia in these or other territories.

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Oppositions have also recently been filed against our European Patent No. 2872488, which claims a crystalline form of roxadustat. Final resolution of the opposition proceedings will take considerable time, and we cannot be assured of the breadth of the claims that will remain in the '488 European patent or that the patent will not be revoked in its entirety.

Furthermore, there is a risk that any public announcements concerning the status or outcomes of intellectual property litigation or administrative proceedings may adversely affect the price of our stock. If securities analysts or our investors interpret such status or outcomes as negative or otherwise creating uncertainty, our common stock price may be adversely affected.

Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.

Our reliance on third-party contractors to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our trade secrets and know-how. Despite the contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations in place with our collaboration partners. Despite our efforts to protect our trade secrets and other confidential information, a competitor's discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

We have an extensive worldwide patent portfolio. The cost of maintaining our patent protection is high and maintaining our patent protection requires continuous review and compliance in order to maintain worldwide patent protection. We may not be able to effectively maintain our intellectual property position throughout the major markets of the world.

The USPTO and foreign patent authorities require maintenance fees and payments as well as continued compliance with a number of procedural and documentary requirements. Noncompliance may result in abandonment or lapse of the subject patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance may result in reduced royalty payments for lack of patent coverage in a particular jurisdiction from our collaboration partners or may result in competition, either of which could have a material adverse effect on our business.

We have made, and will continue to make, certain strategic decisions in balancing costs and the potential protection afforded by the patent laws of certain countries. As a result, we may not be able to prevent third parties from practicing our inventions in all countries throughout the world, or from selling or importing products made using our inventions in and into the U.S. or other countries. Third parties may use our technologies in territories in which we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories which provide inadequate enforcement mechanisms, even if we have patent protection. Such third-party products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the U.S., and we may encounter significant problems in securing and defending our intellectual property rights outside the U.S.*

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries do not always favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop infringement of our patents, misappropriation of our trade secrets, or marketing of competing products in violation of our proprietary rights. In China, our intended establishment of significant operations will depend in substantial part on our ability to effectively enforce our intellectual property rights in that country. Proceedings to enforce our intellectual property rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, and could put our patents in these territories at risk of being invalidated or interpreted narrowly, or our patent applications at risk of not being granted, and could provoke third parties to assert claims against us. We may not prevail in all legal or other proceedings that we may initiate and, if we were to prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Intellectual property rights do not address all potential threats to any competitive advantage we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and intellectual property rights may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- The prosecution of our pending patent applications may not result in granted patents.
- Granted patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product.
- Our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from patent infringement claims for such activities, as well as in countries in which we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in markets where we intend to market our product candidates.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold or used for research under the same or similar names, or similar mechanism of action or product class, but which are sold without proper licenses or approvals, and are often lower cost, lower quality, different potency, or have different ingredients or formulations, and have the potential to damage the reputation for quality and effectiveness of the genuine product. Such products may be used for indications or purposes that are not recommended or approved or for which there is no data or inadequate data with regard to safety or efficacy. Such products divert sales from genuine products. If counterfeit pharmaceuticals illegally sold or used for research result in adverse events or side effects to consumers, we may be associated with any negative publicity resulting from such incidents. Consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. In addition, the use of counterfeit products could be used in non-clinical or clinical studies, or could otherwise produce undesirable side effects or adverse events that may be attributed to our products as well, which could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for the commercialization of our product candidates.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. Except for roxadustat in China for patients on dialysis and not on dialysis, and Japan for patients on dialysis, we have not obtained regulatory approval for any product candidate, and it is possible that neither roxadustat nor pamrevlumab, nor any future product candidates we may discover, in-license or acquire and seek to develop in the future, will obtain regulatory approval in additional countries.

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Our product candidates could fail to receive regulatory approval from the FDA or other regulatory authorities for many reasons, including:

- disagreement over the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement over our interpretation of data from preclinical studies or clinical trials;
- disagreement over whether to accept efficacy results from clinical trial sites outside the U.S. where the standard of care is potentially different from that in the U.S.;
- the insufficiency of data collected from clinical trials of our present or future product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval:
- disapproval of the manufacturing processes or facilities of either our manufacturing plant or third party manufacturers with whom we contract for clinical and commercial supplies; or
- changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or other regulatory authorities may require more information, including additional preclinical or clinical data to support approval, or different analyses, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program altogether. Even if we do obtain regulatory approval, our product candidates may be approved for fewer or more limited indications than we request, approval may be contingent on the performance of costly post-marketing clinical trials, or approval may require labeling that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS or other regulatory authorities may require the establishment of a similar strategy, that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we believe our clinical trials are successful, regulatory authorities may not agree that our completed clinical trials provide adequate data on safety or efficacy. Approval by one regulatory authority does not ensure approval by any other regulatory authority. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for regulatory approvals and even if we file we may not receive the necessary approvals to commercialize our product candidates in any market.

Our relationships with customers, physicians, and third-party payors are subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, health information privacy and security laws, and other healthcare laws and regulations. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

If we obtain approval in the U.S. for any of our product candidates, the regulatory requirements applicable to our operations, in particular our sales and marketing efforts, will increase significantly with respect to our operations and the potential for civil and criminal enforcement by the federal government and the states and foreign governments will increase with respect to the conduct of our business. The laws that may affect our operations in the U.S. include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

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- HIPAA, as amended by Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes certain requirements relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Patient Protection and Affordable Care Act ("PPACA"), which requires manufacturers of drugs, devices, biologics, and medical supplies to report annually to the Centers for Medicare and Medicaid Services ("CMS"), information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;
- foreign and state law equivalents of each of the above federal laws, such as the U.S. Foreign Corrupt Practices Act ("FCPA"), anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and
- the Trade Agreements Act ("TAA"), which requires that drugs sold to the U.S. Government must be manufactured in the U.S. or in TAA approved and designated countries. Drugs manufactured in countries not approved under the TAA, may not be sold to the U.S. without specific regulatory approval. We have little experience with this regulation and there is a risk that drugs made from Chinese-made API may not be sold to an entity of the U.S. such as the Veterans Health Administration ("VA") due to our inability to obtain regulatory approval. While there have been recent VA policy changes that appear to allow for sale of drugs from non-TAA approved countries, this policy may change or there may be additional policies or legislation that affect our ability to sell drug to the U.S. Government.

The scope of these laws and our lack of experience in establishing the compliance programs necessary to comply with this complex and evolving regulatory environment increases the risks that we may unknowingly violate the applicable laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results.

Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have a material adverse effect on our ability to compete in the marketplace.

We are subject to laws and regulations governing corruption, which will require us to develop, maintain, and implement costly compliance programs.

We must comply with a wide range of laws and regulations to prevent corruption, bribery, and other unethical business practices, including the FCPA, antibribery and anti-corruption laws in other countries, particularly China. The implementation and maintenance of compliance programs is costly and such programs may be difficult to enforce, particularly where reliance on third parties is required.

Anti-bribery laws prohibit us, our employees, and some of our agents or representatives from offering or providing any personal benefit to covered government officials to influence their performance of their duties or induce them to serve interests other than the missions of the public organizations in which they serve. Certain commercial bribery rules also prohibit offering or providing any personal benefit to employees and representatives of commercial companies to influence their performance of their duties or induce them to serve interests other than their employers. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

Compliance with these anti-bribery laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the anti-bribery laws present particular challenges in the pharmaceutical industry because in many countries including China, hospitals are state-owned or operated by the government, and doctors and other hospital employees are considered foreign government officials. Furthermore, in certain countries (China in particular), hospitals and clinics are permitted to sell pharmaceuticals to their patients and are primary or significant distributors of pharmaceuticals. Certain payments to hospitals in connection with clinical studies, procurement of pharmaceuticals and other work have been deemed to be improper payments to government officials that have led to vigorous anti-bribery law enforcement actions and heavy fines in multiple jurisdictions, particularly in the U.S. and China.

It is not always possible to identify and deter violations, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

In the pharmaceutical industry, corrupt practices include, among others, acceptance of kickbacks, bribes or other illegal gains or benefits by the hospitals and medical practitioners from pharmaceutical manufacturers, distributors or their third-party agents in connection with the prescription of certain pharmaceuticals. If our employees, affiliates, distributors or third-party marketing firms violate these laws or otherwise engage in illegal practices with respect to their sales or marketing of our products or other activities involving our products, we could be required to pay damages or heavy fines by multiple jurisdictions where we operate, which could materially and adversely affect our financial condition and results of operations. The Chinese government has also sponsored anti-corruption campaigns from time to time, which could have a chilling effect on any future marketing efforts by us to new hospital customers. There have been recent occurrences in which certain hospitals have denied access to sales representatives from pharmaceutical companies because the hospitals wanted to avoid the perception of corruption. If this attitude becomes widespread among our potential customers, our ability to promote our products to hospitals may be adversely affected.

As we expand our operations in China and other jurisdictions internationally, we will need to increase the scope of our compliance programs to address the risks relating to the potential for violations of the FCPA and other anti-bribery and anti-corruption laws. Our compliance programs will need to include policies addressing not only the FCPA, but also the provisions of a variety of anti-bribery and anti-corruption laws in multiple foreign jurisdictions, including China, provisions relating to books and records that apply to us as a public company, and include effective training for our personnel throughout our organization. The creation and implementation of anti-corruption compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. Violation of the FCPA and other anti-corruption laws can result in significant administrative and criminal penalties for us and our employees, including substantial fines, suspension or debarment from government contracting, prison sentences, or even the death penalty in extremely serious cases in certain countries. The SEC also may suspend or bar us from trading securities on U.S. exchanges for violation of the FCPA's accounting provisions. Even if we are not ultimately punished by government authorities, the costs of investigation and review, distraction of our personnel, legal defense costs, and harm to our reputation could be substantial and could limit our profitability or our ability to develop or commercialize our product candidates. In addition, if any of our competitors are not subject to the FCPA, they may engage in practices that will lead to their receipt of preferential treatment from foreign hospitals and enable them to secure business from foreign hospitals in ways that are unavailable to us.

The impact of recent U.S. healthcare reform, its potential partial or full repeal, and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.

The commercial potential for our approved products could be affected by changes in healthcare spending and policy in the U.S. and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") altered Medicare coverage and payments for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. The MMA also provided authority for limiting the number of drugs that will be covered in any therapeutic class and as a result, we expect that there will be additional pressure to reduce costs. For example, the CMS in implementing the MMA has enacted regulations that reduced capitated payments to dialysis providers. These cost reduction initiatives and other provisions of the MMA could decrease the scope of coverage and the price that may be received for any approved dialysis products and could seriously harm our business and financial condition. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies have been enacted in many international markets that could similarly impact the commercial potential for our products.

Under the Medicare Improvements for Patients and Providers Act ("MIPPA"), a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by the CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage. It is unknown whether roxadustat, if approved in the U.S., will be included in the payment bundle. Under MIPPA, agents that have no IV equivalent in the bundle are currently expected to be excluded from the bundle until 2025. If roxadustat were included in the bundle, it may reduce the price that could be charged for roxadustat, and therefore potentially limit our profitability. Based on roxadustat's differentiated mechanism of action and therapeutic effects, and discussions with our collaboration partner, we currently believe that roxadustat might not be included in the bundle and would instead be eligible for a Transitional Drug Add-on Payment Adjustment ("TDAPA") for a 24-month period. After this 24-month period, CMS would determine if roxadustat should be included in the bundle and, if so, what changes to end-stage renal disease prospective payment system reimbursement should be made. If roxadustat is not included in the bundle after the TDAPA period, and would therefore be reimbursed outside of the bundle, it may potentially limit further market penetration of roxadustat.

In March 2010, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, (collectively, the "PPACA"), was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the U.S. There remain judicial and Congressional challenges to certain aspects of the PPACA as well as efforts by the Trump administration to repeal or replace certain aspects of the PPACA. For example, the Tax Cuts and Jobs Act of 2017, (the "Tax Act"), was enacted, which includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Additionally, on December 15, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the PPACA will impact the PPACA and our business.

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Further, in the U.S. there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. At the federal level, the Trump administration's budget proposals for fiscal year 2020 contains further drug price control measures that could be enacted during the budget process or in other future legislation. In addition, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services has solicited feedback on some of these measures and has implemented others under its existing authority. While some of these measures may require additional authorization to become effective, the U.S. Congress and the Trump administration have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that additional U.S. healthcare reform measures will be adopted in the future, any of which could limit the amount

Roxadustat is considered a Class 2 substance on the 2019 World Anti-Doping Agency Prohibited List that could limit sales and increase security and distribution costs for us and our partners.*

Roxadustat is considered a Class 2 substance on the World Anti-Doping Agency ("WADA") Prohibited List. There are enhanced security and distribution procedures we and our collaboration partners and third-party contractors will have to take to limit the risk of loss of product in the supply chain. As a result, our distribution, manufacturing and sales costs for roxadustat, as well as for our partners, will be increased which will reduce profitability. In addition, there is a risk of reduced sales due to patient access to this drug.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could result in significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failure to:

- comply with FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or comparable foreign regulatory authorities;
- comply with manufacturing standards we have established;
- comply with privacy laws protecting personal information;
- comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities;
- comply with the FCPA and other anti-bribery laws;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, delays in clinical trials, or serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could harm our business, results of operations, financial condition and cash flows, including through the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations applicable to our operations in the U.S. and foreign countries. These current or future laws and regulations may impair our research, development or manufacturing efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our International Operations

We are establishing international operations and seeking approval to commercialize our product candidates outside of the U.S., in particular in China, and a number of risks associated with international operations could materially and adversely affect our business.*

We expect to be subject to a number of risks related with our international operations, many of which may be beyond our control. These risks include:

- different regulatory requirements for drug approvals in different countries;
- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain countries;
- changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems and different competitive drugs indicated to treat the indications for which our product candidates are being developed;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- compliance with the FCPA, and other anti-corruption and anti-bribery laws;
- U.S. and foreign taxes, including income, excise, customs, consumption, withholding, and payroll taxes;
- foreign currency fluctuations, which could result in increased operating costs and expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- a reliance on CROs, clinical trial sites, principal investigators and other third parties that may be less experienced with clinical trials or have different methods of performing such clinical trials than we are used to in the U.S.;
- potential liability resulting from development work conducted by foreign distributors; and
- business interruptions resulting from geopolitical actions specific to an international region, including war and terrorism, or natural disasters, including the differing impact of the COVID-19 pandemic on each region.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. Refer to "Business — Government Regulation — Regulation in China" for a discussion of the regulatory requirements that are applicable to our current and planned business activities in China. In recent years, the regulatory framework in China regarding the pharmaceutical industry has undergone significant changes, and we expect that it will continue to undergo significant changes. For example, the Chinese government has implemented regulations that impact distribution of pharmaceutical products in China. These regulations generally require that at most two invoices may be issued throughout the distribution chain. Failure to comply with the "Two-Invoices" regulations would prevent us from accessing the market in China. We are establishing a jointly owned Distribution Entity with AstraZeneca to manage distribution in China, and there are complexities involved in establishing proper systems to perform distribution with which we have limited experience. We expect to continue to manage distribution in certain provinces in China. We have limited experience managing distribution of pharmaceutical products, and this new distribution structure may impose higher costs or limit or delay our ability to sell products to our principal customers, and may limit the near term sales of our products. Any other such changes or amendments may result in increased compliance costs to our business or cause delays in or prevent the successful development or commercialization of our product candidates in China. Any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China.

We plan to use our own manufacturing facilities in China to produce roxadustat API and roxadustat drug product. As an organization, we have limited experience in the construction, licensure, and operation of a manufacturing plant, and accordingly we cannot assure you we will be able to continually meet regulatory requirements to operate our plant and to sell our products.*

We have two manufacturing facilities in China, with one located in Beijing and the other in Cangzhou, Hebei. However, as an organization, we have limited experience licensing and operating commercial manufacturing facilities.

We will be obligated to comply with continuing cGMP requirements and there can be no assurance that we will maintain all of the appropriate licenses required to manufacture our product candidates for clinical and commercial use in China. In addition, we and our product suppliers must continually spend time, money and effort in production, record-keeping and quality assurance and appropriate controls in order to ensure that any products manufactured in our facilities meet applicable specifications and other requirements for product safety, efficacy and quality and there can be no assurance that our efforts will continue to be successful in meeting these requirements.

Manufacturing facilities in China are subject to periodic unannounced inspections by the NMPA and other regulatory authorities. We expect to depend on these facilities for our product candidates and business operations in China. Natural disasters or other unanticipated catastrophic events, including power interruptions, water shortages, storms, fires, pandemics (including the COVID-19 pandemic), earthquakes, terrorist attacks, government appropriation of our facilities, and wars, could significantly impair our ability to operate our manufacturing facilities. Certain equipment, records and other materials located in these facilities would be difficult to replace or would require substantial replacement lead-time that would impact our ability to successfully commercialize our product candidates in China. The occurrence of any such event could materially and adversely affect our business, financial condition, results of operations, cash flows and prospects.

In addition to manufacturing, we are responsible for pharmacovigilance, medical affairs, and management of the third-party distribution logistics for roxadustat in China. We have no experience in these areas as a company, and accordingly we cannot assure you we will be able to meet regulatory requirements or operate in these capacities successfully.

We are responsible for commercial manufacturing, pharmacovigilance, medical affairs, and management of the third-party distribution logistics (with AstraZeneca through the Distribution Entity) for roxadustat commercial activities in China. While we have been increasing our staffing in these areas, as a company, we have no experience managing or operating these functions for a commercial product and there can be no guarantee that we will do so efficiently or effectively. Mistakes or delays in these areas could limit our ability to successfully commercialize roxadustat in China, could limit our eventual market penetration, sales and profitability, and could subject us to significant liability in China.

We and our collaboration partner in China, AstraZeneca, may experience difficulties in successfully generating sales of roxadustat in China.

We and AstraZeneca have a profit sharing arrangement with respect to roxadustat in China and any difficulties we may experience in generating sales will affect our bottom line. Difficulties may be related to our ability to maintain reasonable pricing and reimbursement, obtain hospital listing, or other difficulties related to distribution, marketing, and sales efforts in China. For example, our current National Reimbursement Drug List reimbursement pricing is effective for a standard two-year period (between January 1, 2020 to December 31, 2021), after which time we will have to renegotiate a new price for roxadustat, which may be lower. Sales of roxadustat in China may be limited due to the complex nature of the healthcare system, low average personal income, pricing controls, still developing infrastructure and potentially rapid competition from other products. The hospital listing process is critical to roxadustat's near-term commercial success in China and may take many years to obtain the majority of hospital listings.

The retail prices of any product candidates that we develop may be subject to control, including periodic downward adjustment, by Chinese government authorities.

The price for pharmaceutical products is highly regulated in China, both at the national and provincial level. Price controls may reduce prices to levels significantly below those that would prevail in less regulated markets or limit the volume of products that may be sold, either of which may have a material and adverse effect on potential revenues from sales of roxadustat in China. Moreover, the process and timing for the implementation of price restrictions is unpredictable, which may cause potential revenues from the sales of roxadustat to fluctuate from period to period.

If our planned business activities in China fall within a restricted category under the China Catalog for Guidance for Foreign Investment, we will need to operate in China through a variable interest entity ("VIE") structure.

The China Catalog for Guidance for Foreign Investment sets forth the industries and sectors that the Chinese government encourages and restricts with respect to foreign investment and participation. The Catalog for Guidance for Foreign Investment is subject to revision from time to time by the China Ministry of Commerce. While we currently do not believe the development and marketing of roxadustat falls within a restricted category under the Catalog for Guidance for Foreign Investment, if roxadustat does fall under such a restricted category, we will need to operate in China through a VIE structure. A VIE structure involves a wholly foreign-owned enterprise that would control and receive the economic benefits of a domestic Chinese company through various contractual relationships. Such a structure would subject us to a number of risks that may have an adverse effect on our business, including that the Chinese government may determine that such contractual arrangements do not comply with applicable regulations, Chinese tax authorities may require us to pay additional taxes, shareholders of our VIEs may have potential conflicts of interest with us, and we may lose the ability to use and enjoy assets held by our VIEs that are important to the operations of our business if such entities go bankrupt or become subject to dissolution or liquidation proceedings. VIE structures in China have come under increasing scrutiny from accounting firms and the Securities and Exchange Commission ("SEC") staff. If we do attempt to use a VIE structure and are unsuccessful in structuring it so as to qualify as a VIE, we would not be able to consolidate the financial statements of the VIE with our financial statements, which could have a material adverse effect on our operating results and financial condition.

FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.*

We plan to conduct all of our business in China through FibroGen China Anemia Holdings, Ltd. and FibroGen Beijing. We may rely on dividends and royalties paid by FibroGen Beijing for a portion of our cash needs, including the funds necessary to service any debt we may incur and to pay our operating costs and expenses. The payment of dividends by FibroGen Beijing is subject to limitations. Regulations in China currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in China. FibroGen Beijing is not permitted to distribute any profits until losses from prior fiscal years have been recouped and in any event must maintain certain minimum capital requirements. FibroGen Beijing is also required to set aside at least 10.0% of its after-tax profit based on Chinese accounting standards each year to its statutory reserve fund until the cumulative amount of such reserves reaches 50.0% of its registered capital. Statutory reserves are not distributable as cash dividends. In addition, if FibroGen Beijing incurs debt on its own behalf in the future, the agreements governing such debt may restrict its ability to pay dividends or make other distributions to us. As of June 30, 2020, approximately \$11.9 million of our cash and cash equivalents is held in China.

Any capital contributions from us to FibroGen Beijing must be approved by the Ministry of Commerce in China, and failure to obtain such approval may materially and adversely affect the liquidity position of FibroGen Beijing.

The Ministry of Commerce in China or its local counterpart must approve the amount and use of any capital contributions from us to FibroGen Beijing, and there can be no assurance that we will be able to complete the necessary government registrations and obtain the necessary government approvals on a timely basis, or at all. If we fail to do so, we may not be able to contribute additional capital to fund our Chinese operations, and the liquidity and financial position of FibroGen Beijing may be materially and adversely affected.

We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.

Most of our product sales will occur in local Chinese currency and our operating results will be subject to volatility from currency exchange rate fluctuations. To date, we have not hedged against the risks associated with fluctuations in exchange rates and, therefore, exchange rate fluctuations could have an adverse impact on our future operating results. Changes in value of the Renminbi against the U.S. dollar, Euro and other currencies is affected by, among other things, changes in China's political and economic conditions. Currently, the Renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. Any significant currency exchange rate fluctuations may have a material adverse effect on our business and financial condition.

In addition, the Chinese government imposes controls on the convertibility of the Renminbi into foreign currencies and the remittance of foreign currency out of China for certain transactions. Shortages in the availability of foreign currency may restrict the ability of FibroGen Beijing to remit sufficient foreign currency to pay dividends or other payments to us, or otherwise satisfy their foreign currency-denominated obligations. Under existing Chinese foreign exchange regulations, payments of current account items, including profit distributions, interest payments and balance of trade, can be made in foreign currencies without prior approval from the State Administration of Foreign Exchange ("SAFE") by complying with certain procedural requirements. However, approval from SAFE or its local branch is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The Chinese government may also at its discretion restrict access in the future to foreign currencies for current account transactions. If the foreign exchange control system prevents us from obtaining sufficient foreign currency to satisfy our operational requirements, our liquidity and financial position may be materially and adversely affected.

Because FibroGen Beijing's funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen Beijing deposits its funds could adversely affect our business.

Banks and other financial institutions in China do not provide insurance for funds held on deposit. As a result, in the event of a bank failure, FibroGen Beijing may not have access to funds on deposit. Depending upon the amount of money FibroGen Beijing maintains in a bank that fails, its inability to have access to cash could materially impair its operations.

We may be subject to tax inefficiencies associated with our offshore corporate structure.*

The tax regulations of the U.S. and other jurisdictions in which we operate are extremely complex and subject to change. New laws, new interpretations of existing laws, such as the Base Erosion Profit Shifting project initiated by the Organization for Economic Co-operation and Development, and any legislation proposed by the relevant taxing authorities, or limitations on our ability to structure our operations and intercompany transactions may lead to inefficient tax treatment of our revenue, profits, royalties, and distributions, if any are achieved.

In addition, we and our foreign subsidiaries have various intercompany transactions. We may not be able to obtain certain benefits under relevant tax treaties to avoid double taxation on certain transactions among our subsidiaries. If we are not able to avail ourselves to the tax treaties, we could be subject to additional taxes, which could adversely affect our financial condition and results of operations.

On December 22, 2017, the Tax Cuts and Jobs Act (Tax Act) was enacted which instituted various changes to the taxation of multinational corporations. Since inception, various regulations and interpretations have been issued by governing authorities and we continue to examine the impacts to our business, which could potentially have a material adverse effect on our business, results of operations or financial conditions.

Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.

We seek to protect the products and technology that we consider important to our business by pursuing patent applications in China and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. We note that the filing of a patent application does not mean that we will be granted a patent, or that any patent eventually granted will be as broad as requested in the patent application or will be sufficient to protect our technology. There are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications not to be granted, including known or unknown prior art, deficiencies in the patent application, or lack of originality of the technology. Furthermore, the terms of our patents are limited. The patents we hold and the patents that may be granted from our currently pending patent applications have, absent any patent term adjustment or extension, a twenty-year protection period starting from the date of application.

Intellectual property rights and confidentiality protections in China may not be as effective as those in the U.S. or other countries for many reasons, including lack of procedural rules for discovery and evidence, low damage awards, and lack of judicial independence. Implementation and enforcement of China intellectual property laws have historically been deficient and ineffective and may be hampered by corruption and local protectionism. Policing unauthorized use of proprietary technology is difficult and expensive, and we may need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability and validity of our proprietary rights or those of others. The experience and capabilities of China courts in handling intellectual property litigation varies and outcomes are unpredictable. An adverse determination in any such litigation could materially impair our intellectual property rights and may harm our business.

Uncertainties with respect to the China legal system could have a material adverse effect on us.

The legal system of China is a civil law system primarily based on written statutes. Unlike in a common law system, prior court decisions may be cited for reference but are not binding. Because the China legal system continues to rapidly evolve, the interpretations of many laws, regulations and rules are not always uniform and enforcement of these laws, regulations and rules involve uncertainties, which may limit legal protections available to us. Moreover, decision makers in the China judicial system have significant discretion in interpreting and implementing statutory and contractual terms, which may render it difficult for FibroGen Beijing to enforce the contracts it has entered into with our business partners, customers and suppliers. Different government departments may have different interpretations of certain laws and regulations, and licenses and permits issued or granted by one government authority may be revoked by a higher government authority at a later time. Navigating the uncertainty and change in the China legal system will require the devotion of significant resources and time, and there can be no assurance that our contractual and other rights will ultimately be enforced.

Changes in China's economic, political or social conditions or government policies could have a material adverse effect on our business and operations.

Chinese society and the Chinese economy continue to undergo significant change. Changes in the regulatory structure, regulations, and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy, but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the regulatory structure and structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes and structural changes, any of which could materially and adversely affect FibroGen Beijing's development and commercialization timelines, liquidity, access to capital, and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China. In addition, the changing government regulations and policies could result in delays and cost increases to our development, manufacturing, approval, and commercialization timelines in China.

Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may materially and adversely affect our business, financial condition and results of operations.

We are subject to China Labor Contract Law, which provides strong protections for employees and imposes many obligations on employers. The Labor Contract Law places certain restrictions on the circumstances under which employers may terminate labor contracts and require economic compensation to employees upon termination of employment, among other things. In addition, companies operating in China are generally required to contribute to labor union funds and the mandatory social insurance and housing funds. Any failure by us to comply with Chinese labor and social insurance laws may subject us to late fees, fines and penalties, or cause the suspension or termination of our ability to conduct business in China, any of which could have a material and adverse effect on business, results of operations and prospects.

Developments relating to the United Kingdom's referendum vote in favor of leaving the European Union could adversely affect us.

Effective January 31, 2020, the United Kingdom commenced an exit from the European Union, commonly referred to as "Brexit." During a transition period (set to expire on December 31, 2020), the British government will continue to negotiate the terms of the United Kingdom's future relationship with the European Union. The outcome of these negotiations is uncertain, and we do not know to what extent Brexit will ultimately impact the business and regulatory environment in the United Kingdom, the rest of Europe, or other countries. The effects of the United Kingdom's withdrawal from the European Union, and the perceptions as to its impact, are expected to be far-reaching and may adversely affect business activity and economic conditions in Europe and globally and could continue to contribute to instability in global financial markets, including foreign exchange markets. The United Kingdom's withdrawal from the European Union could also have the effect of disrupting the free movement of goods, services and people between the United Kingdom and Europe and could also lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which European laws to replace or replicate, including laws that could impact our ability, or our collaborator's ability in the case of roxadustat, to obtain approval of our products or sell our products in the United Kingdom. Changes impacting our ability to conduct business in the United Kingdom or other European countries, or changes to the regulatory regime applicable to our operations in those countries (such as with respect to the approval of our product candidates), may materially and adversely impact our business, prospects, operating results, and financial condition.

Risks Related to the Operation of Our Business

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, commercialization and administration capabilities or contract with third parties to provide these capabilities for us. As our operations expand and we continue to undertake the efforts and expense to operate as a public reporting company, we expect that we will need to increase the responsibilities on members of management in order to manage any future growth effectively. Our failure to accomplish any of these steps could prevent us from successfully implementing our strategy and maintaining the confidence of investors in us.

Loss of senior management and key personnel could adversely affect our ability to successfully develop our product candidates, conduct our clinical trials and commercialize our product candidates.*

We are highly dependent on members of our senior management team, including Enrique Conterno, our Chief Executive Officer. The loss of the services of Mr. Conterno or any of our senior management could significantly impact the development and commercialization of our products and product candidates and our ability to successfully implement our business strategy.

Recruiting and retaining qualified commercial, development, scientific, clinical, and manufacturing personnel are and will continue to be critical to our success, particularly as we expand our commercialization operations. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

There is also significant competition, in particular in the San Francisco Bay Area, for the hiring of experienced and qualified personnel, which increases the importance of retention of our existing personnel. If we are unable to continue to attract and retain personnel with the quality and experience applicable to our product candidates, our ability to pursue our strategy will be limited and our business and operations would be adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our product candidates.

We face an inherent risk of product liability as a result of the clinical testing, manufacturing and commercialization of our product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under state consumer protection acts. If we are unable to obtain insurance coverage at levels that are appropriate to maintain our business and operations, or if we are unable to successfully defend ourselves against product liability claims, we may incur substantial liabilities or otherwise cease operations. Product liability claims may result in:

- · termination of further development of unapproved product candidates or significantly reduced demand for any approved products;
- material costs and expenses to defend the related litigation;
- a diversion of time and resources across the entire organization, including our executive management;
- product recalls, withdrawals or labeling restrictions;
- termination of our collaboration relationships or disputes with our collaboration partners; and
- reputational damage negatively impacting our other product candidates in development.

If we fail to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, we may not be able to continue to develop our product candidates. We maintain product liability insurance in a customary amount for the stage of development of our product candidates. Although we believe that we have sufficient coverage based on the advice of our third-party advisors, there can be no assurance that such levels will be sufficient for our needs. Moreover, our insurance policies have various exclusions, and we may be in a dispute with our carrier as to the extent and nature of our coverage, including whether we are covered under the applicable product liability policy. If we are not able to ensure coverage or are required to pay substantial amounts to settle or otherwise contest the claims for product liability, our business and operations would be negatively affected.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, collaboration partners, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We upgraded our disaster and data recovery capabilities in 2017, however, to the extent that any disruption or security breach, in particular with our partners' operations, results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and it could result in a material disruption and delay of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

We depend on sophisticated information technology systems to operate our business and a cyber-attack or other breach of these systems could have a material adverse effect on our business.

We rely on information technology systems to process, transmit and store electronic information in our day-to-day operations. The size and complexity of our information technology systems makes them vulnerable to a cyber-attack, malicious intrusion, breakdown, destruction, loss of data privacy or other significant disruption. While we have recently upgraded our disaster data recovery program, a successful attack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyber-attacks are becoming more sophisticated and frequent. We have invested in our systems and the protection and recoverability of our data to reduce the risk of an intrusion or interruption, and we monitor and test our systems on an ongoing basis for any current or potential threats. There can be no assurance that these measures and efforts will prevent future interruptions or breakdowns. If we fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to these systems, we could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating costs and expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows.

Our headquarters are located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business, results of operations and financial condition.*

We and some of the third-party service providers on which we depend for various support functions are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires, and has been affected by the COVID-19 pandemic, including economic disruption resulting from the related shelter-in-place and stay-at-home governmental orders.

After a comprehensive earthquake risk analysis conducted by Marsh Risk, we decided not to purchase earthquake or flood insurance. Based upon (among other factors) the Marsh Risk analysis, the design and construction of our building, the expected potential loss, and the costs and deductible associated with earthquake and flood insurance, we chose to self-insure. However, earthquakes or other natural disasters could severely disrupt our operations, or have a larger cost than expected, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, or otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place are unlikely to provide adequate protection in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events, such as the COVID-19 pandemic. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above your purchase price.

In general, pharmaceutical, biotechnology and other life sciences company stocks have been highly volatile in the current market. The volatility of pharmaceutical, biotechnology and other life sciences company stocks is sometimes unrelated to the operating performance of particular companies and biotechnology and life science companies stocks often respond to trends and perceptions rather than financial performance. In particular, the market price of shares of our common stock could be subject to wide fluctuations in response to the following factors:

- results of clinical trials of our product candidates, including roxadustat and pamrevlumab;
- the timing of the release of results of and regulatory updates regarding our clinical trials;
- the level of expenses related to any of our product candidates or clinical development programs;
- results of clinical trials of our competitors' products;
- safety issues with respect to our product candidates or our competitors' products;
- regulatory actions with respect to our product candidates and any approved products or our competitors' products;
- fluctuations in our financial condition and operating results, which will be significantly affected by the manner in which we recognize revenue from the achievement of milestones under our collaboration agreements;
- adverse developments concerning our collaborations and our manufacturers;
- the termination of a collaboration or the inability to establish additional collaborations;
- the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- · changes in legislation or other regulatory developments affecting our product candidates or our industry;

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- fluctuations in the valuation of the biotechnology industry and particular companies perceived by investors to be comparable to us;
- speculation in the press or investment community;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- activities of the government of China, including those related to the pharmaceutical industry as well as industrial policy generally;
- performance of other U.S. publicly traded companies with significant operations in China;
- changes in market conditions for biopharmaceutical stocks; and
- the other factors described in this "Risk Factors" section.

As a result of fluctuations caused by these and other factors, comparisons of our operating results across different periods may not be accurate indicators of our future performance. Any fluctuations that we report in the future may differ from the expectations of market analysts and investors, which could cause the price of our common stock to fluctuate significantly. Moreover, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources and could also require us to make substantial payments to satisfy judgments or to settle litigation.

If securities or industry analysts do not continue to publish research or reports about our business, or if they change their recommendations regarding our stock adversely, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of the analysts who cover us downgrade our stock, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to regularly publish reports on us, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exercise significant influence over matters subject to stockholder approval.*

As of July 31, 2020, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 40.03% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date and shares issuable upon settlement of restricted stock units that will vest within 60 days after such date. This percentage is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G, if any, filed with the SEC, which information may not be accurate as of January 31, 2020. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. The interests of this group may differ from those of other stockholders and they may vote their shares in a way that is contrary to the way other stockholders vote their shares. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

We may engage in future acquisitions that could disrupt our business, cause dilution to our stockholders and harm our business, results of operations, financial condition and cash flows and future prospects.

We may, in the future, make acquisitions of, or investments in, companies that we believe have products or capabilities that are a strategic or commercial fit with our present or future product candidates and business or otherwise offer opportunities for us. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our existing stockholders' percentage of ownership;
- incur debt and assume liabilities; and
- incur amortization expenses related to intangible assets or incur large and immediate write-offs.

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We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products or technologies, or employees or other assets of the acquisition target;
- increases to our expenses;
- disclosed or undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- reprioritization of our development programs and even cessation of development and commercialization of our current product candidates;
- harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current directors or management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a majority
 of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed prior to the end of their term only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- require a supermajority vote of the holders of our common stock or the majority vote of our board of directors to amend our bylaws; and
- require a supermajority vote of the holders of our common stock to amend the classification of our board of directors into three classes and to amend certain other provisions of our certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

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Moreover, because we are incorporated in Delaware, we are governed by certain anti-takeover provisions under Delaware law which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. We are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Changes in our tax provision or exposure to additional tax liabilities could adversely affect our earnings and financial condition.*

As a multinational corporation, we are subject to income taxes in the U.S. and various foreign jurisdictions. Significant judgment is required in determining our global provision for income taxes and other tax liabilities. In the ordinary course of a global business, there are intercompany transactions and calculations where the ultimate tax determination is uncertain. Our income tax returns are subject to audits by tax authorities. Although we regularly assess the likelihood of adverse outcomes resulting from these examinations to determine our tax estimates, a final determination of tax audits or tax disputes could have an adverse effect on our results of operations and financial condition.

We are also subject to non-income taxes, such as payroll, excise, customs and duties, sales, use, value-added, net worth, property, gross receipts, and goods and services taxes in the U.S., state and local, and various foreign jurisdictions. We are subject to audit and assessments by tax authorities with respect to these non-income taxes and may have exposure to additional non-income tax liabilities, which could have an adverse effect on our results of operations and financial condition.

In addition, our judgment in providing for the possible impact of the Tax Act remains subject to developing interpretations of the provisions of the Tax Act. As regulations and guidance evolve with respect to the Tax Act, we continue to examine the impact to our tax provision or exposure to additional tax liabilities, which could have a material adverse effect on our business, results of operations or financial condition.

Tariffs imposed by the U.S. and those imposed in response by other countries, as well as rapidly changing trade relations, could have a material adverse effect on our business and results of operations.

Changes in U.S. and foreign governments' trade policies have resulted in, and may continue to result in, tariffs on imports into and exports from the U.S. Throughout 2018 and 2019, the U.S. imposed tariffs on imports from several countries, including China. In response, China has proposed and implemented their own tariffs on certain products, which may impact our supply chain and our costs of doing business. If we are impacted by the changing trade relations between the U.S. and China, our business and results of operations may be negatively impacted. Continued diminished trade relations between the U.S. and other countries, including potential reductions in trade with China and others, as well as the continued escalation of tariffs, could have a material adverse effect on our financial performance and results of operations.

Our amended and restated certificate of incorporation designates the state or federal courts located in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.*

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the federal district courts of the United States of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolvin

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain and you may never receive a return on your investment.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in our product candidates and maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS.

Use of Proceeds from Initial Public Offering of Common Stock

On November 13, 2014, our Registration Statement on Form S-1, as amended (Reg. Nos. 333-199069 and 333-200189) was declared effective in connection with the initial public offering of our common stock. There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on November 14, 2014.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES.

Not applicable.

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CERTIFICATION

- I, Enrique Conterno, certify that;
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e)) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f)) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 6, 2020

/s/ Enrique Conterno
Enrique Conterno
Chief Executive Officer
(Principal Executive Officer)

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CERTIFICATION

- I, Pat Cotroneo, certify that;
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e)) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f)) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 6, 2020

/s/ Pat Cotroneo

Pat Cotroneo

Senior Vice President, Finance and Chief Financial Officer (Principal Financial Officer)

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended ("Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Enrique Conterno, Chief Executive Officer of FibroGen, Inc. ("the Company"), and Pat Cotroneo, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

- 1. The Company's Quarterly Report on Form 10-Q for the period ended June 30, 2020, to which this Certification is attached as Exhibit 32.1 ("Periodic Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and
- 2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: August 6, 2020

In Witness Whereof, the undersigned have set their hands hereto as of the 6th day of August, 2020.

/s/ Enrique Conterno	/s/ Pat Cotroneo		
Enrique Conterno	Pat Cotroneo		
Chief Executive Officer	Senior Vice President, Finance and		
	Chief Financial Officer		

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of FibroGen, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

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Call Participants

EXECUTIVES

Enrique A. Conterno *CEO & Director*

ANALYSTS

Joel Lawrence Beatty *Citigroup Inc., Research Division*

Presentation

Joel Lawrence Beatty

Citigroup Inc., Research Division

Hi, everyone. Thanks for joining the session with FibroGen. I'm pleased to have with us the CEO, Enrique Conterno. Enrique, thanks for joining us today.

Enrique A. Conterno

CEO & Director

No, thank you very much, Joe. I very much appreciate the invitation. Look forward to discussing a number of topics.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Yes. Great. So I guess, I think a lot of viewers are going to be familiar with FibroGen, but some may not. So could you begin with an overview of what the key areas of focus are for FibroGen?

Enrique A. Conterno

CEO & Director

Sure. So FibroGen is a company very much based in science. We've been able to progress 2 key products, one of them, roxadustat. The second one, pamrevlumab, which are very much in late stages. Roxa has already been commercialized in China and Japan and undergoing review in the U.S., Europe. And pamrevlumab has now 3 studies in clinical -- 3 programs in Phase III in clinical development in IPF, which is idiopathic, pulmonary fibrosis, Duchenne muscular dystrophy and finally, in locally unresectable pancreatic cancer -- locally advanced unresectable pancreatic cancer. In addition to that, I think we are making a concerted effort to really advance new products into the clinic. We are delighted to have announced that Percy Carter is joining FibroGen to lead our scientific efforts. We're very excited about that.

So it's -- the focus for FibroGen is really around fibrotic diseases, cancer and, of course, anemia, given roxadustat program.

Question and Answer

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. So a lot of great topics in there to discuss over the next 45 minutes or so. But let's begin with the topic that I think is probably at the top of a lot of investors' minds, and that's the vadadustat results that came out last week from Akebia in non-dialysis setting that seemed disappointing. But could you discuss your take on those results? And what that means for roxadustat?

Enrique A. Conterno

CEO & Director

Yes, I think, there are 3 elements that I would highlight as we think about those results and in the context for roxa. I think number one, I think, is the significant level of evidence that we have already with roxadustat around NDD. As you know, when we look at our pool studies for NDD, we were able to show non-inferiority relative to placebo, which is a higher bar than a comparison to a product that had -- or product to have box warnings. So we feel very good about our pool MACE data in NDD.

Second, in addition to the pool studies, we have an additional study, DOLOMITES, which is a study against an active comparator, darbepoetin, where we adjudicated MACE events. And in that study, when we look at time to MACE events, we basically had a hazard ratio of 0.81 in favor of roxadustat. So favorable trend in favor for roxadustat, an additional study.

And then finally, I would highlight that -- which I think is important to put in context. But when it comes to cardiovascular studies, we've seen there's ample precedent for the FDA to basically label the products with their corresponding outcomes from CV, meaning different outcomes even within the same class, then we'll have different labels. We, of course, have -- see this in GLP-1s, where we've seen a number of different studies. Some GLP-1 have protective claims when it comes to CV, some do not. Some have different populations. So we see though the specific results for each product basically reflected on each of their respective labels. That's not only the case for GLP-1, so we can think about SGLT2s or DPP-4s, where we basically see the MACE data reflected of those -- of the specific results for the molecules.

We think that's also how investors should be thinking about roxadustat and the results that we have, meaning not all HIFs necessarily are the same, so we have our own evidence and we feel very good about the level of evidence that we have with roxadustat.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Very good. And maybe one -- I'll ask it about a little bit more is the DOLOMITES data. And I know that there's a lot of studies that FibroGen has on roxadustat that go under this package. If I have them straight, I think DOLOMITES isn't necessarily part of the main core U.S. studies and was conducted to just help support -- I think it may have been requested by Europe. But could you share a little bit more about how much is able -- is that still submitted to FDA? How much are they able to look at that and consider that now?

Enrique A. Conterno

CEO & Director

Yes. So the FDA -- for purposes of MACE, I think the FDA basically requested a particular way of us pulling certain studies because in NDD, all of our studies were against placebo. DOLOMITES is against an active comparator. It's difficult to combine apples and oranges because you're having different levels of comparison. So our submission basically reflected the 3 studies that we have relative to placebo and basically the MACE -- the adjudicated MACE outcomes and looking at safety from that perspective.

DOLOMITES is an additional study. And yes, we submit all of the information that we have to the FDA, including a study that may not be part of the pool studies, but basically, the FDA gets to see all of our data.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Okay. Great. And then in the -- some of this relates to labeling. And I think a discussion that's come up a lot with investors, even before the data we saw last week is could roxadustat have a black box warning. And I know that at this point, we're getting close to the PDUFA date in December. So there's probably not a lot you can say on that. But maybe just generally, how important is this debate even to have? Is it important to roxadustat whether it has a black box warning or not?

Enrique A. Conterno

CEO & Director

Yes. So we commented as part of the Q3 -- Q2 earnings call that unfortunately, given it was imminent that we would be entering labeling discussions that we were not going to be able to make further comments in terms of our engagement with the FDA. So that is the case. We feel -- I think what I can say is we feel very good about where we are in terms of the review with the FDA, the level of engagement that we have. I know this question about a box warning comes often, which is are we going to get one or not. My -- and what is the impact that a box warning would have? It's always difficult to handicap what is going to be the final level. But we feel very good about the level of energy that we have. I think what I've said before is that we have excellent data. We don't believe that the data that we have warrants a box warning. But once again, difficult to handicap what we'll end up with the FDA.

What I would say is that it is not only whether you have a box warning or not, but also what does the box warning say. There are ample examples out there where products that have box warnings basically have done incredibly well in terms of having commercial success. There is one condition, which I think is met in the case of roxadustat, but it's difficult for a product that has a box warning if the competitors in the class don't have one. I think the uptake and the overall commercial ability to be highly successful commercially is -- can be impaired. But in this particular case, we are entering a field where products do have a box warning in the case of ESAs. So it is not a limiting factor. I don't think it limits the overall long-term success of the product. Box warning may limit some of the initial uptick, but long term, I think we have ample of evidence that we see these products are very much as a transformational medicine.

Joel Lawrence Beatty

Citigroup Inc., Research Division

That's great. So let's pivot away from labeling. And maybe could I ask about reimbursement and focusing on the dialysis setting and that's unique that there's the bundled payment system that many patients are under in the U.S. and then there's also the TDAPA program that could cover the first couple of years or so, I believe. Could you tell us about the process generally for roxadustat, and see if it's eligible for TDAPA and when you find out about that?

Enrique A. Conterno

CEO & Director

Yes. So we believe that roxa will be eligible for -- TDAPA is eligible for TDAPA once it is approved. I think the process is once we receive approval, we will submit a request something called -- that is called a HCPCS code and then submit for TDAPA reimbursement. We think it is critical for us to be prepared to do this as soon as we get approval so that we can get the reimbursement for TDAPA as soon as possible. We believe that reimbursement could come as early as April 1 because we see now CMS that could be -- is, from a guidance perspective, making decisions on a quarterly basis. So I think the idea -- best-case scenario for us to be -- and I think also something that is likely is that for us to shoot to have reimbursement from a TDAPA perspective starting April 1 of next year. Clearly, this is critically important because it is an incentive for -- that CMS is providing for dialysis organizations to be able to include products that deliver innovation into their protocols. And in a certain way, it's almost -- it eliminates any type of economic disincentive not to include products.

So -- and as you mentioned, it -- TDAPA, according to the guidance today, would last for a period of 2 years. So I think it is critically important for us, and we're working to ensure that we get reimbursement through TDAPA as soon as possible.

Joel Lawrence Beatty

Citigroup Inc., Research Division

That sounds great. And April 1 day just comes a few months after the December PDUFA date. So that seems like nice timing. And then can I ask what happens after that 2-year period of TDAPA? Do we know if roxadustat would be in the bundle or not? Or what -- how do you figure out what happens after those 2 years?

Enrique A. Conterno

CEO & Director

I think the concept under TDAPA and the concept behind the 2 years is that CMS will basically review the experience with roxadustat based on those 2 years and the benefits that roxadustat offers. And then I think the intent will be to try to think about how to include basically roxadustat or HIF-PHIs into the bundle and what the appropriate rate for the bundle will be based on that experience and the benefit that they've seen with the innovation.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. So let's switch to non-dialysis. Could you just -- could you help frame the size of the addressable market? And I ask because for dialysis patients, it seems like there's a lot of great data out there that makes them pretty easy to count. But I don't think the same is true for non-dialysis. So how do you think about the size of that market?

Enrique A. Conterno

CEO & Director

Yes. The way I think about the size is for us to be able to look at patients with CKD and anemia, and we are looking at stages mainly 3 to 5. And we are -- we need to be thinking about, okay, what is the size of that overall population. I think roughly, you can estimate that in the U.S., there are about maybe 5 million patients with CKD and anemia in total. Now this is anemia defined at higher levels that in terms of hemoglobin that we will be able to treat with roxa. So we need to -- when we think about the addressable market for roxa, it's maybe half of that size. So I think about an overall universe of our addressable market of about 2.5 million patients that could be potentially treated with roxadustat in that setting.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Got it. So the 2.5 million seems to be I think higher than where ESAs are at right now in non-dialysis patients. But certainly, they have a long history of their own issues. Can you maybe help frame the perspective of what could help grow the non-dialysis market opportunity beyond where ESAs are at right now?

Enrique A. Conterno

CEO & Director

Yes. So today, I think most patients with CKD and anemia in non-dialysis setting actually are not treated with an ESA. In fact, when you look at data, looking at the 12 months prior to going on dialysis, you look at maybe about -- only about 14% of those patients have been treated with ESA. So what that basically means that there's a huge opportunity to basically be able to activate and be able to treat many more patients that are suffering from anemia. The opportunity here is one of market expansion. And we are thinking not about an increase of 10% or 20%, but we're thinking about a multiple increase relative to the opportunity.

Keep in mind that prior to ESAs getting some of those negative trials in NDD when it comes to certain levels of hemoglobin targets and so forth, the rate of treatment was nearly 30%. Today, the rate of treatment is less than half of that, with CKD and anemia, specifically on the NDD setting. So there's a very good past history that there's a need to be able to treat patients. And we think that roxadustat, therefore, can be an important catalyst for the market expansion. So we think this is a very relevant and important opportunity for us.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Terrific. So FibroGen seems to have a presence all over the world in one way or another, and one very common area is China. Roxadustat is already on the market there. And earlier this year, we saw sales increase from \$5 million in Q1 to about \$16 million in Q2, which was a nice increase. Could you describe a little bit what was behind that increase? And how to think about that trajectory going forward?

Enrique A. Conterno

CEO & Director

Yes. We're very pleased with the increase that we saw in terms of revenues with roxa in China. Clearly, as you know, we received NRDL inclusion, effective at the start of this year. So the first couple of quarters have been terrific, \$5 million and \$15.7 million, respectively. I think what we see in an underlying metric that is very important for trying to think about long-term success for the product is basically how well the hospital listings are progressing. And we mentioned that at the end of Q2, our hospital listings in China because once -- yes, you can have national reimbursement, but then you need to list hospital to hospital.

But our hospital listings are -- today -- as at the end of Q2, represented already 45% of the overall CKD anemia opportunity in China. Quite frankly, that is a very significant number. The progress is excellent. You can look at a number of benchmarks or products that have become blockbusters and what were they able to achieve the first couple of quarters relative to -- in terms of coverage. So we feel that we made already significant progress.

Listing is a particularly important metric to look at because it is not like hospitals can just list products. Anytime a hospital lists a product, they actually have to -- in China, you have to exclude a product. So you are, in a sense, making a trade-off. So we feel very good about the products that we make. In addition to that is when we look at the adoption that we have, I think we feel very good about not just the overall adoption the hospitals are -- that different prescribers are having, but also about the breadth of different patients. It's not just dialysis patients, but we basically look at the breadth of patients that physicians are choosing for roxadustat, everything from home dialysis to NDD. And if there is a probably an area where we've been surprised is how quickly we've seen adoption in the NDD segment in China. So we're very pleased with that. And I think it provides -- I think the breadth of patients provides, what I say, a number of different ways, levers for us to grow long term. It's a great predictor of long-term success.

Joel Lawrence Beatty

Citigroup Inc., Research Division

That's great. So a lot of great points in there in terms of hospital listings and the breadth of patients that are on roxadustat. The non-dialysis point was interesting that you've seen growth there. And maybe a little bit early there in the launch to ask this question, but what do you see as the adherence like in non-dialysis patients? Do they just take it, address their anemia and stop? Or is it the type of thing that they're continuing?

Enrique A. Conterno

CEO & Director

It's always difficult -- first, it's always difficult to measure and look at length of therapy in a specific setting because you need longitudinal data. We have expected that adherence in the dialysis setting is going to be very good and more challenging in non-dialysis setting, just because you're part of the protocol on the dialysis setting and it's -- it can be administered even during the dialysis session. So when it comes to NDD, that is going to be a key focus for us to ensure how can we ensure not just that we have enough

patients being started on roxadustat, but how do we ensure that the length of therapy is appropriate and how when we do that, we can make that as long as possible. I think it's too early for us to comment on that, but that's something that we are looking at carefully and something that we'll be able to comment more in the future.

Joel Lawrence Beatty

Citigroup Inc., Research Division

That's great. So one more question on China. And during the Q2 earnings, you announced that there is the, I think, a revised agreement with AstraZeneca. Could you tell us more about the key points of what's new in that agreement?

Enrique A. Conterno

CEO & Director

Sure. So I think it was an opportunity for AstraZeneca and FibroGen to basically update the China agreement. I think for FibroGen, I think first, for both parties, I think it better aligns both parties to ensure that we are maximizing the opportunity that we have with roxa. In particular for FibroGen, I think our overall profitability becomes more predictable and improved with the new agreement. So we -- that's something that was important to us as well.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Okay. Very good. So for roxa, just maybe moving away from anemia of chronic kidney disease, there's also other areas of focus. Could you provide an update on the status in those -- I think there's 2 other main areas, MDS and chemotherapy-induced anemia. Tell us about...

Enrique A. Conterno

CEO & Director

Yes. So we have disclosed those 2 studies, and we're also looking at additional potential opportunities within the anemia space with roxadustat. But specifically, when it comes to MDS and CIA, MDS is now in Phase III and trial is enrolling. So we expect to complete enrollment next year. We'll be providing very specific time lines on each one of our trials for roxa and pam at the Q3 earnings call.

CIA, for us, chemo-induced anemia, is a much larger opportunity. Almost when we look at relative size, almost comparable to what we think an anemia CKD is, so very significant opportunity. We're in Phase II, and we are enrolling very well, and hopefully, we'll be fully enrolled this year. So we want to be enrolled as soon as possible and then thinking about, of course, starting the Phase III based on those results.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. And so next month is ASN. FibroGen certainly had a big presence there last year with their data. Are you able to share anything about what to expect from FibroGen next month at ASN?

Enrique A. Conterno

CEO & Director

Yes. We expect a record presence at ASN. I think a key part of our preparation for launch is ensuring that we have all of our data out there. So we are expecting about 40 different types of presentations at ASN that's record-breaking for us. And that includes about 10 oral presentations and then posters and so forth. So very, very significant presence.

In addition to ASN for us, it is critical that we basically publish our key studies, both individual studies that have been conducted, but also some of the pool analysis when it comes to safety, when it comes to MACE, both in DD and NDD, but also in incident dialysis, the pool incident dialysis MACE study. So all of that is very much in progress. We made most, if not all, of the submission when it comes to publications of all

of these key studies, and we expect all of them are going to be published by the end of the year, prior to launch.

Joel Lawrence Beatty

Citigroup Inc., Research Division

That's great. And 40 presentations is striking, and I think it makes me reminisce of the old days not too long ago, trying to run around and catch 40 different presentations in person at one meeting, but the times have changed and hopefully, we can catch them all virtually.

Enrique A. Conterno

CEO & Director

Yes. I think one thing that sometimes maybe is underappreciated with roxadustat is we've conducted so many studies, right? And many of them are long-term studies when it comes to -- because we were looking at cardiovascular outcomes. So there's a lot of possibility for us to mine that data. Some of those analysis, of course, are post hoc, but they're interesting for us to be able to look at a number of different elements of those studies. It's very exciting. There's a lot of learning. And I think I see a lot of different elements and a lot of different value that I think roxadustat can provide to patients.

Joel Lawrence Beatty

Citigroup Inc., Research Division

That's great. So maybe let's switch gears to pamrevlumab. And recently, you started a trial in COVID for that agent. Can you tell us a little bit about what we might have learned from a trial in that setting?

Enrique A. Conterno

CEO & Director

Yes. As -- we basically started 2 trials in COVID, one in Italy. The Italian trial is investigator-initiated trial. So we are, of course, providing the product and so forth, but it is different from the trial in the United States, where we are the formal sponsor of that Phase II trial. Keep in mind that when it comes to COVID, we are looking at 2 different types of trials within COVID. One of them is the acute phase and also, we're looking at the post-hospitalization phase for patients that develop fibrosis in the lungs and the ability for pamrevlumab to be able to help with that. Clearly, we have the IPF data that gives us a lot of confidence.

On the trial that we started is the acute trial. I'll be honest, I think it's very challenging to enroll in that trial right now, given the hundreds of trials that are involved when it comes to acute COVID and also some new therapies that people believe are already helping. So enrollment is extremely challenging in that specific trial.

When it comes to the chronic trial, we feel that so the -- post the acute phase for -- and we think about helping patients with their fibrosis. We feel that, that trial will be much easier to enroll, but I think it is critical for us that we have good alignment with the FDA on the type of design and the endpoints for this trial so that we can continue to develop and eventually, hopefully, even make it to market. We feel a good level of conviction in the trial given the IPF data that we've seen.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. Maybe on that last point, what timing in the process do you look for the alignment with FDA?

Enrique A. Conterno

CEO & Director

I think at the time that we are designing the study, we want to make sure that the evidence that we have is going to be adequate for us to be able to move quickly. Clearly, this is a -- when we look at that -- those specific patients, there are no treatments, of course. So we are in a certain way, plowing new ground. So agreement with the FDA on the specific endpoints, I think, is going to be critical. It's not just us looking at that, you can imagine products in the IPF space are also thinking about that. And my sense is just given

that level of discussion that we had with the FDA is that many of those sponsors are also having some very similar discussions with the FDA.

Joel Lawrence Beatty

Citigroup Inc., Research Division

That's great. As you think about pamrevlumab and lung disease. And I think one of the unique things about the IPF data set for pamrevlumab is the imaging data that showed improvements in HRCT. Is there a potential to see something like that in COVID patients or not given that disease, how does that work?

Enrique A. Conterno

CEO & Director

Yes. We think so that -- I think it's an advantage to pam because when it comes -- given that we have underlying improvements in fibrosis, so we want to really make sure that we can look at imaging data. Imaging data is important for to -- from a level of earnings perspective, but the FDA also looks for more functional endpoints, so clinical endpoints. Clearly, when it comes to IPF, it is forced vital capacity as the accepted primary endpoint. I think it's difficult for -- it has been difficult for the FDA to approve products for fibrosis merely on imaging. I think it's an additional aspect that basically support the biology of the product, the effect of the product and the underlying disease. And as you said, I think it's critically important because I think foundationally, we are basically impacting the progression of the disease.

So all of that is important, but the FDA will look for functional endpoint. It's important that we have alignment on those.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Got it. So maybe switching to IPF. It seems like IPF and chronic lung diseases, in general, has been a really tough area for enrolling in clinical trials nowadays with COVID. How is enrollment going in your IPF program?

Enrique A. Conterno

CEO & Director

I think it's a challenge, as you well said, I think patients with IPF are particularly vulnerable to COVID. So we actually decided to pause our studies back in March. We restarted not long ago some of those studies. So what we did in the meantime that we basically paused enrollment of our studies, we first wanted to ensure the continued integrity of the trial, meaning for patients that were already on pamrevlumab had been enrolled ensuring the continuity of care and safety of those patients in a clinical trial. I think we managed that well. Importantly, also is how do we make sure that once we're able to restart enrollment, which is where we are now, how do we put ourselves in the best position to enroll quickly. And I think we've done a very nice job in terms of activating new sites for IPF when it comes to ZEPHYRUS 1.

So we've expanded the number of sites in the U.S., also outside of the U.S. And in particular, in areas where we see COVID under control, we are seeing good enrollment like South Korea and so forth. We have a second IPF trial, which is expected to start very soon, ZEPHYRUS 2, which looks at mainly enrollment in Europe. And we also have a very good plan for us to activate all of those sites as guickly as possible.

Clearly, this is an area of focus for us when it comes to enrollment. We'll be providing very specific time lines for each one of our trials with pamrevlumab and roxadustat at the Q3 earnings call in terms of what are the next milestones and when do we expect data readouts and so forth.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. Let's see. So I think maybe on that point, with pancreatic cancer and DMD Phase III trials, I think are also underway. I think with DMD just moving ahead in the last few days or so. I think it's on a press release. It sounds like you'll have more to share later on, but maybe could you tell us a little bit about those?

Enrique A. Conterno

CEO & Director

I can. I think LAPC, I think, is enrolling well. So we feel good about how that trial is enrolling right now. Clearly, I think focus for us has been also site activation. And I think we've made a lot of progress as well on the site activation side. I think that we are in a very good position to enroll that quickly. And I view the trial as highly valuable, not only in the trial itself and the level of confidence given the results that we saw in Phase II, but also I think the optionality that, that trial provides, when it comes to additional indications related to pancreatic cancer, whether it's maintenance or whether it's metastatic. So I feel very good about the opportunities that, that trial specifically gives us.

When it comes to DMD, we just started, I think the focus right now is site activation and, of course, some enrollment. But we feel very good about the ability to enroll in that population quickly. Those patients with DMD also are particularly vulnerable to COVID-19. So we need to be -- we need to take all the appropriate precautions and makes it a little more challenging to enroll as well. But we have to realize also those patients don't have many options, and we think that pamrevlumab is a product that can truly make a difference for those patients.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. So maybe circling back to IPF. I believe that the Phase III program is designed as a monotherapy program. Could you share a little bit about the implications of taking that approach, maybe in terms of enrollment in clinical trials as well as the commercial opportunity, if approved?

Enrique A. Conterno

CEO & Director

Yes. Keep in mind, when we looked at our Phase II data for IPF, I think the data is, in my opinion, spectacular and that when we look at the data, we show basically an effect size that is unmatched. It's better than any product that is standard of care today or any product in development. Our Phase III basically try to replicate that. Why are we starting it that way and the implications for enrollment? Clearly, from an enrollment perspective, it becomes more challenging to either involve naive patients or patients naive to treatment or patients that are -- that have failed on the standard of care. So yes, it is more difficult to enroll. But I think the opportunity, given what we think the effect size could be for pamrevlumab, I think, it's very significant. And that we feel that not only that we can have a very large effect size in Phase III, just like we showed in Phase II when it comes to forced vital capacity. But in addition to that, we believe that we can show an impact in the underlying disease and of course, imaging helps with that, but also some of the measures that we look at that, including mortality, of course.

So all in all, I think we feel that if the data from Phase II is replicated into Phase III that we will have a product that will be used as standard of care. And I think the question then is, what product should accompany that product, if at all, but we want to create in pamrevlumab the standard for IPF.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Great. So maybe let's take a step back and look at maybe some questions about the larger company as a whole. And one is, as you mentioned in your opening remarks, FibroGen created a new role for a Chief Scientific Officer and made a hire there. Can you characterize maybe the timing and importance of that? And what's the -- I think there's just so much talk about FibroGen as this clinical stage company, but what's going on in the preclinical research and development nowadays?

Enrique A. Conterno

CEO & Director

Yes. I think it's fair to say, I think the company has been focused on our late-stage products for quite some time, given the progress that we made when it comes to clinical development. But I think we have to realize that FibroGen is in a unique position when it comes to the type of science that we are advancing.

I think it's fair to say that we are a leading company -- the leading company when you have to HIF biology and when it comes to CTGF biology. And both scientific platforms, well, they have yielded a products. In the case of roxadustat, already commercially available in China and Japan and under review. In the case of pamrevlumab in Phase III, the opportunities to leverage the understanding of the biology and our expertise is very significant. So I see multiple opportunities. Sometimes, when I say that people say, well, are you develop -- planning to develop other HIF-PHIs, maybe, but I'm thinking beyond HIF-PHIs. And we -- our aim in terms of -- and our goal with recruiting Percy Carter is to -- as our new Chief Scientific Officer is really to give all of our efforts when it comes to research the type of leadership that our science warrants, which is we are really -- we really want to invest behind our research and bring new products into the clinic. And we think given the platform, the scientific platform that we have, we have a great opportunity to do so.

I think this is very much an underappreciated part of the FibroGen story and one that I think can create huge future value for the company and for patients.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Very good. And so another question I'd like to ask you is what -- and FibroGen has quite a bit of cash when you look at -- I think it was \$716 million in cash at the end of last quarter, but then there's also milestones that seem pretty likely to come, I think, it's \$245 million of milestones over the next 12 months. So that gets to, I think, just under \$1 billion when we put that all together. Any plans for that cash going forward?

Enrique A. Conterno

CEO & Director

Yes. I think the position that FibroGen has, I think, is very strong from a cash perspective. Keep in mind that when we look at our investments, when we look at roxadustat, for example, all of our clinical development and commercial expenses outside of China are really paid by our partners. So we're in a position that we are going to be growing revenue and so forth and basically receiving a royalty in the low 20s. When it comes to China, of course, it's 50-50, but we expect China will be profitable soon. So we have a unique position with roxadustat. In addition to roxa, then, of course, we're making the investments in pam, in research. But the reality is that we expect to build cash over time.

I think your question, if I understand it, is, okay, what do you plan to do with that cash? And right now, I think the focus for us has to be in advancing roxa and making it commercially highly successful, developing and accelerating the development of pamrevlumab to make that a real product with significant benefits across different indications, all of which are -- offer significant value to patients and to FibroGen overall, reignite all of our research. So our internal agenda, I think, is very important.

I will view any type of external efforts right now as a bit distracting given the amount of value we believe we can create organically. That doesn't mean that maybe 9 months from now, 12 months from now, so I'm going to be thinking about what opportunities do we have for that cash. But the timing right now is for us to focus on our execution internally created much value from these programs that can create significant amount of value and then look at maybe 12 months from now, what opportunities do we have strategically. So we think about strengthening the position of the company.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Very good. And I -- we have a couple of minutes left. So I thought I'd squeeze in a question that came in as we were doing this call. And it's a little bit more of a -- more details about the TDAPA payment. And I know that's something you need to sort of file for, so maybe too early to ask. But can you share a little bit more about how those details would work and -- such as would it be like a whole payment to reimburse for the cost of HIF in and of itself or would taken to some -- account some differential with ESAs, how does that work?

Enrique A. Conterno

CEO & Director

Yes. I think the regulation today basically looks at TDAPA, basically and that the -- this add-on payments that TDAPA represents basically is qualified as been 100% of the ASP, of the average selling price. So you're going to look at different channels, what the average selling price is in those channels, and that basically become this add-on payment for TDAPA. So there's no offset for the TDAPA payment for not using an ESA or -- well, that is going to be the case, there's no such offset. So in a certain way, it's an important incentive, right, for inclusion of innovation and best-in-class therapies into the dialysis protocols of this -- of the different dialysis organizations.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Got it. And I guess maybe another question related to pricing. And I know it's not something you've shared yet on details on pricing. But would the -- the price for dialysis patients and the price for non-dialysis patients inherently have to be the same or given the different dynamics there, would they be different?

Enrique A. Conterno

CEO & Director

Yes. I mean I won't be commenting on pricing strategy and so forth. But I think if you are asking about the list price, list price is going to be the same for the product. The product will be utilized in different settings. But I -- at this point in time, I think we don't intend to provide much of a commentary when it comes to price setting or price strategy until basically the time of launch.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Yes. It totally makes sense. And I think that wraps up the time that we have today. So I really appreciate the discussion. It covered a lot of great topics and ended up being great timing to have this discussion today. So Enrique, thanks very much.

Enrique A. Conterno

CEO & Director

Joe, thank you very much. I very much appreciate the time today.

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EXHIBIT FF

S&P Global
Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Wednesday, September 16, 2020 8:30 PM GMT

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Enrique A. Conterno *CEO & Director*

ANALYSTS

Albert Hwang; Morgan Stanley; Managing Director

Presentation

Albert Hwang; Morgan Stanley; Managing Director

Good afternoon, everybody. Thank you for joining. This is the FibroGen fireside chat. I'm Albert Hwang from Morgan Stanley. Thanks for being at the conference. And I'd like to introduce the CEO of FibroGen, Enrique Conterno, who -- maybe you can give a couple of minute overview on how things are going with the company. And then we can get started with questions. Enrique?

Enrique A. Conterno

CEO & Director

Very good. Thank you, Albert. Thank you very much for the invitation. We have an exciting agenda here at FibroGen. Clearly, roxadustat being commercialized in China and Japan, very much undergoing the final stages of the regulatory review in the United States, submission in Europe. Clearly, a transformational medicine when it comes to CKD anemia.

We are making progress with pamrevlumab on enrollments on a collective of high need medical indications whether it's IPF or LAPC or DMD. So now we basically have Phase III programs in each one of those indications. And I would say we're very excited when we think about IPF, I think, our Phase II data. And what we have, I think, is superb. So very excited about that particular asset.

And finally, I think we are really putting a lot of effort behind our overall research agenda, bringing new products into the clinic here at FibroGen, and recently, we hired a new Chief Scientific Officer, Percy Carter. I'm very excited about the opportunity to truly make innovation, a constant stream here at FibroGen bringing new molecules into the clinic. So I'm very excited with an agenda across all fronts. Albert, I think you are on mute, right now.

Question and Answer

Albert Hwang; Morgan Stanley; Managing Director

They always tell you to mute, and then I always forget. So we'll get into detail on all of those fronts. I think maybe the first thing to focus on is probably a question that's on everybody's minds. And that is how do you think about roxa as different from vada, the Akebia product, given their recent non -- NDD data? So do you look at that as a -- every drug is specific to its own targets? Or do you look at it as a mechanism effect, et cetera?

Enrique A. Conterno

CEO & Director

Yes. Clearly, that's a question that is coming often to us, and I'll provide, I think, an appropriate perspective in terms of trying to put that result into context for investors. I'd like to make 3 points. Number one, roxadustat has a very significant data set in MDD. We have a pool analysis in NDD that we submitted to the FDA. As part of our NDD pool analysis, when we look at MACE, we were non-inferior relative to placebo, which is a higher bar than ESAs would be. So we feel very good about our data there.

Point two is we -- in addition to that post study, we have an additional study, DOLOMITES, against an active comparator in darbepoetin. That study had MACE outcomes adjudicated. And as part of those results, we saw a MACE result that was favorable to roxadustat, a hazard ratio of 0.81 in that specific DOLOMITES study. So that's an important additional level of evidence, I think, in favor of roxadustat and the safety when it comes to NDD.

Finally, I think it's a question that comes, okay, the data that roxa has is very strong in NDD, but what are going to be the implications from a labeling perspective, given this data. And I think here, I will point out that the FDA -- there's ample pressure by the FDA to look at cardiovascular studies for different products, even when they're within the same class and make sure that the label applies for those products comes from the respective cardiovascular studies that we have when it comes to GLP-1s, cardiovascular studies that were, in some cases, different in results, and you see the labels basically reflect the outcome and the data for each study and the label for that product. That is also the case for GLP-2s of DPP-4s. So we take that to mean that the cardiovascular studies are really vast studies with many patients. And the FDA takes the results from those studies seriously and basically, in summary, applies the respective outcome from the study to the specific product, the specific label.

In short, what I would mention when it comes to our data is that we continue to feel very confident about our prospects overall for us roxadustat, and, of course, specifically in the NND setting given the data that we have.

Albert Hwang; Morgan Stanley; Managing Director

Okay. And your PDUFA date, just to remind everyone, is December 20 of this year. And the package that you put together for the FDA, and please share what you're comfortable with but, is mostly the 6 studies, 3 for NDD and 3 for DD, and is there any additional data that, you mentioned that you have this additional trial, I think you said it was a DOLOMITES one, that has the comparator with darbe? Would that information be shared as well? Do you try to share as much as possible? Or how does that work?

Enrique A. Conterno

CEO & Director

Yes. I think when it comes to the submission to the FDA, we agreed with the FDA prior to submission on the studies that will be pooled for MACE, 3 specific studies when it comes to DD and 3 specific studies when it comes to NDD. And we have also agreed on the statistical method of how we were going to look at MACE on those studies.

Clearly, when it comes to the submission to the FDA, we include all of our studies. So the ones that are pooled for MACE as well as some of the additional studies that we may have conducted. So yes, I think the DOLOMITES data that we had at that time was also submitted to the FDA.

Albert Hwang; Morgan Stanley; Managing Director

Okay. Great. Okay. So we'll -- I'm sure everybody will be looking forward to the December PDUFA.

Maybe moving on to China. I think it would be helpful to just talk about how the China business is doing broadly after launch. And perhaps if you can talk about what the read-through could be for the U.S. and rest of the world? And if that is a read-through or how things are different or how things are harder or easier in China?

Enrique A. Conterno

CEO & Director

Yes. As you are aware, we got reimbursement in China. Starting this year, we are in the NRDL. Post NRDL, I think key critical success factor for launches to ensure listings in hospitals. And we've done a fantastic job. I think -- AstraZeneca is our partner in China, we basically have a 50-50 profit share for the roxa business in China with AstraZeneca. They've done a fantastic job really listing roxadustat in many hospitals. So we made a lot of progress.

At the end of Q2, we were already listed in hospitals that represented 45% of the overall CKD anemia opportunity in China, and that's very impressive. We had \$5 million in sales in Q1, \$15.7 million in Q2. And we see continuous progression when it comes to revenue, demand that we basically see. So the underlying business, I think, is very strong in China. We are very pleased with the progress that we have.

We, of course, look at China and the -- on its own merit in terms of this can be a blockbuster product, just looking at China alone. So a very significant opportunity for us with roxadustat in China. And -- but of course, we also try to learn from China, what can we apply to other markets, including the U.S. So we capture a lot of those learnings. Of course, the adoption that we have for roxadustat in China is brings -- give us a lot of confidence in terms of what we could expect in other geographies.

So one of the learnings or things that we've seen in China is we've seen probably faster uptake in NDD than maybe at least than I had expected. So -- which is, I think, very encouraging. And when we look at the broad use of roxadustat in China, whether it's home dialysis, dialysis in general or late-stage NDD or NDD in general, we -- I basically see lots of opportunities for roxadustat to grow over the long term. A great opportunity for us to capitalize in China, and we've got to capture those learnings and apply them in the U.S. when relevant.

Albert Hwang; Morgan Stanley; Managing Director

I think it will be helpful to just highlight some of the key numbers in terms of addressable market. Obviously, there's a much bigger population, but at least I'm not familiar with is the dialysis population similar to the U.S.? Is it higher or lower? What about non-dialysis? And how has that been growing? Or how has that been changing?

Enrique A. Conterno

CEO & Director

Yes. So the dialysis market in China is actually the largest dialysis market in the world. We estimate somewhere 700,000 to 800,000 patients on dialysis alone. We see that market growing pretty fast year-on-year. In fact, in China, there's 1 million to 2 million additional dialysis-eligible patients that should be maybe or could be in dialysis, but are not in dialysis today.

In addition to that, we estimate that the market in China could be maybe an additional 5 million patients when it comes to NDD, as we think about the addressable market for us in China. So it's really a really significant opportunity and I would highlight that we are basically going to be the only HIF who are really creating this new market, but the only HIF for quite some time. We don't expect other HIFs until maybe 2024. So great opportunity for us to build a great business, I think, in China.

Albert Hwang; Morgan Stanley; Managing Director

Okay. Great. And can you maybe remind us of the partnership with AZ? And how much you contribute to the sales and marketing? Or how -- I guess, how you're educating yourself for other markets through the maturity of the China piece?

Enrique A. Conterno

CEO & Director

Yes. So allow me maybe to provide a broad perspective on roxa partnership and then I'll specifically address China. But when we think about roxadustat, basically, all of our commercial and development expenses, so new indications, as you know, we are pursuing chemo-induced anemia. We're pursuing MDS, potentially other additional indications beyond those. All of those expenses really are paid by our partners. When we think about commercial expenses, similar.

So everything basically, expenses development or commercial outside of China are paid by the partners. In China, we basically go 50-50 with AstraZeneca, where we have a 50-50 profit share. In the rest of the markets, we are under a royalty transfer price type of arrangement, where we're getting a royalty in the low to mid-20 in terms of percentage. So it's very attractive for us. We have a major transformation of products, and we are very active, of course, in China, given the 50-50 share.

We're trying to rely on the strengths of AstraZeneca in China, so they do much of that -- or all of the sales and marketing efforts. And in our case, it's basically medical and the science and the things that FibroGen could contribute best. So I think the arrangement of the partnership, the collaboration in China, I think, is working well. We recently updated our agreement in China with AstraZeneca to better align both parties, which I think is excellent, that, that agreement provides more predictable and better profitability also for Fibro.

Albert Hwang; Morgan Stanley; Managing Director

Great. Okay. And hopefully, as that business grows, the -- and your investor base will start to see more of the value that, that produces and I guess the synergies that it has with the rest of the business.

Maybe moving on to pamrev. Can you just very quickly highlight the asset, the mechanism before we get into some of the questions, just what it is, what you're going after?

Enrique A. Conterno

CEO & Director

Sure. Pamrevlumab is a monoclonal antibody basically an anti-CTGF. CTGF is a major fibrotic pathway. And really, we have an asset in Phase III, in 3 different indications now in Phase III. And we're very much excited about by some of the data that we've seen. Clearly, IPF, idiopathic pulmonary fibrosis, is a very important indication for pamrevlumab. In IPF, we had outstanding Phase II data I mentioned, and I highlight that our Phase II data, I believe, is -- the effect size that we saw on our Phase II data is better than any data that I've seen with IPF that I'm aware of on products that are either marketed, that today are standard of care or products that are in development.

So very excited about the ability to have an asset with a very differentiated profile. The key for us with that asset is execution and ensuring enrollment. We made a lot of progress when it comes to site activation over the last few months. But clearly, enrollment right now, in particular, because of COVID and the vulnerability of this specific population is a challenge. But I feel good about our ability to recruit quickly now that we have all those sites activated.

We also have LAPC, locally advanced pancreatic cancer, another exciting opportunity for us. We had the Phase II data that was promising. Clearly, here, we are looking at improving the resectability of the patients that are on the pamrevlumab arm, and there's a lot of evidence that shows that improved resectability, you're able to resect, survival improves in oncology. So great opportunity for us with that indication.

And finally, with DMD, we just started that trial in DMD.

Our Phase II trial in DMD was open-label, and we did not have a comparator, but when we look at the progression of the disease in those patients, it is -- we're very encouraged by what we see.

So each one of these indications alone is very significant, but collectively, I think it's a massive opportunity for FibroGen and great opportunity for patients.

Albert Hwang; Morgan Stanley; Managing Director

Okay. And on the IPF side, you touched on it previously. Has the COVID environment impacted enrollment? I know a lot of pulmonary companies, patients tend to stay at home. Has that impacted you? And how do you see that going forward? Or how have you been trying to mitigate that?

Enrique A. Conterno

CEO & Director

Yes. So yes, we do see that. And clearly, in fact, we actually paused enrollment formally on the trial for a few months. And even to this day, we have a number of sites that are still not enrolling based on a decision that they've made at that site due to COVID.

Clearly, this is very much understandable given the vulnerability of these patients, in particular, to COVID-19. There are number of things that we've done. First, I think let's utilize this time to ensure that we can have as many sites activated so that when the situation with COVID improve, we can be hitting on all cylinders when it comes to enrollment. So that's one. We've done geographic expansion of pam in IPF and also in LAPC. So we've looked at a number of additional countries. And we've also expanded in some of these countries. And in fact, as we look at our enrollment in places where, for example, South Korea, where COVID is much more contained, we actually see a very good enrollment with pam. We are --we've gotten approval to conduct a trial in China. So that's also coming. So we're going to be hitting on all cylinders. I think we've prepared ourselves well to ensure that we can recruit as quickly as we can.

Albert Hwang; Morgan Stanley; Managing Director

Okay. And just as you think about the IPF strategy going forward, you are enrolling for naive patients or Esbriet experienced or combination? Can you describe that trial?

Enrique A. Conterno

CEO & Director

Yes. We are enrolling both naive patients and also patients that have been treated with the standard of care and maybe failed or could not tolerate the standard of care. So we're treating both types of patients depending on the different trial, also depending on the country. This particular strategy, I think, is manageable and doable for us given what we see the profile of -- the pamrevlumab could have, meaning given the large effect size that we can have. We also believe that the upside for this product is for surely to be modifying from a disease progression perspective.

We've seen, of course, imaging from our Phase II trial, and that's really unique data where we basically see basically improvements in fibrosis. So my -- if all of the stars align here, I think we could have truly a product that not only shows good outcomes when it comes to forced vital capacity, which is the typical outcome for products in IPF, but actually has a unique opportunity to show improvements when it comes to disease progression itself. And if we do that, I think sky is the limit.

Albert Hwang; Morgan Stanley; Managing Director

Okay. Great. And for all of these programs, what are some of the near-term milestones? Or when can we expect you to give guidance on milestones for these?

Enrique A. Conterno

CEO & Director

Yes. So stay tuned because we plan to provide some of those time lines soon. We have highlighted that we expect to provide time lines on each one of our programs at the Q3 earnings call. So you should expect

time lines when it comes to each one of the pamrevlumab Phase III studies and the roxa MDS and CIA studies. We do intend to provide those milestones and timing.

Albert Hwang; Morgan Stanley; Managing Director

Okay. I guess -- and kind of bigger picture corporate. Since you've joined in the beginning of the year, you've made a few key hires. Can you talk a little bit about what you've done and where you plan on taking the company with those key hires?

Enrique A. Conterno

CEO & Director

Yes. Clearly, I think we made a number of key hires, some that are pretty public, some that are -- that we are continuing to strengthen our bench strength here at FibroGen. I think the 2 that you're referring to are our Chief Commercial Officer and our Chief Scientific Officer. I'm delighted that both Thane Wettig and Percy Carter, respectively, have joined FibroGen. Clearly, FibroGen is transitioning from being just a purely development company to also have a commercial presence. Not only with -- of course, with roxa, but we need to start planning for pamrevlumab as well. So that's critically important.

And I had the chance to work directly with Thane for over 10 years. So I'm delighted that he and I are working together again. And then Percy Carter, Percy has a very -- an important storied career. BMS and most recently, Janssen. And I think that is a reflection that we want top talent to be coming to FibroGen. In this particular case, a reflection of our aim that we have with our overall scientific and research agenda and to be able to leverage the size that we have when it comes to HIF biology, CTGF biology and bring new products into the clinic. So very excited about both hires and the value that they could add to our agenda at FibroGen and ultimately to patients.

Albert Hwang; Morgan Stanley; Managing Director

Okay. So the Chief Commercial Officer understood your PDUFA date coming up. The Chief Science Officer -- is there more that we expect to see from FibroGen beyond pamrev and roxa?

Enrique A. Conterno

CEO & Director

Absolutely. So I think that's the entire idea. I think our aim is to be able to deliver a constant stream of innovation coming from our preclinical efforts. And clearly, the proof of the pudding is how well can we build a pipeline, a clinical pipeline, and I'm excited with the experience and the level of expertise and leadership that Percy Carter will be able to bring to FibroGen.

Albert Hwang; Morgan Stanley; Managing Director

Okay. Great. Okay. Well, we have a few minutes left. I thought maybe I'd give you a chance to talk about anything that I've missed. I think I've gotten the questions in the queue answered. And just an overall closing remarks.

Enrique A. Conterno

CEO & Director

Yes. No, it's an exciting time for us. Clearly, we are in the final stages of basically a regulatory process in the United States. Clearly, our commercial preparations are in full swing.

Reimbursement in the United States will be key. We feel that we have a clear path towards reimbursement in both the dialysis setting and the non-dialysis setting. In the dialysis setting, we expect to be eligible for TDAPA reimbursement. This is an additional payment over and above the bundle. And we are planning and preparing to apply for the TDAPA reimbursement as soon as we get approval through AstraZeneca.

So TDAPA, just to remind you, is basically an additional payment that the organization will receive as a result of using roxadustat, that is based on 100% of the average selling price. So excited about that opportunity.

And we believe that our reimbursement to TDAPA could be effective as early as April 1, given the time lags that we basically expect. So clearly, reimbursement is key in both dialysis and the non-dialysis setting for roxa. We have made a number of changes to improve our enrollment when it comes to our pam studies. I'm highly confident on some of the changes that were made and the impact that, that could have in ensuring faster enrollment that has been typical.

And stay tuned for what -- we expect to have an Analyst Day, Analyst Meeting in Q1 of next year, where we expect to showcase a lot more of all of our plans, including some of the plans that we basically have when it comes to research.

Albert Hwang; Morgan Stanley; Managing Director

Okay. Great. It looks like you're going to have busy next couple of quarters. So wish you the best of luck. And thank you for taking the time today.

Enrique A. Conterno

CEO & Director

Thank you very much, Albert. Very much appreciate it.

Albert Hwang; Morgan Stanley; Managing Director Okay. All right. Bye-bye.

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EXHIBIT GG

S&P Global Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN FQ3 2020 Earnings Call Transcripts

Thursday, November 05, 2020 10:00 PM GMT

S&P Global Market Intelligence Estimates

	-FQ3 2020-			-FQ4 2020-	-FY 2020-	-FY 2021-
	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS	CONSENSUS	CONSENSUS
EPS Normalized	(0.81)	0.35	NM	(0.16)	(2.81)	(0.76)
Revenue (mm)	61.49	44.03	V (28.39 %)	131.56	271.93	487.47

Currency: USD

Consensus as of Oct-29-2020 1:25 AM GMT

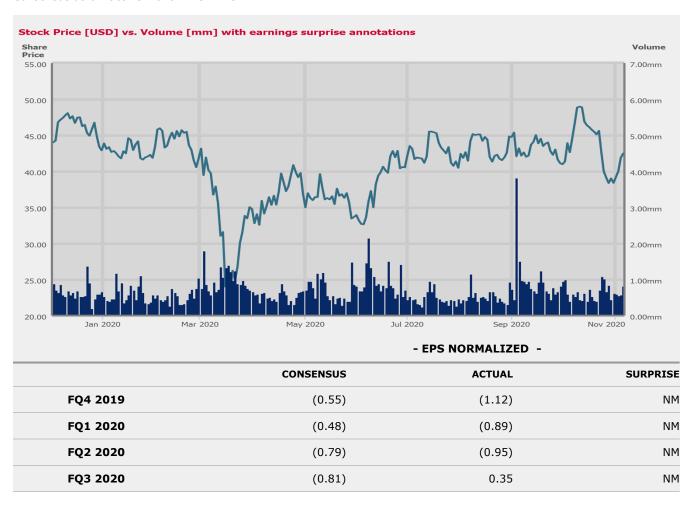


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EXECUTIVES

Christine L. Chung Senior Vice President of China Operations

Enrique A. Conterno CEO & Director

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Michael Tung Investor Relations Executive

Pat CotroneoChief Financial Officer

Thane Wettig *Chief Commercial Officer*

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Michael Jonathan Yee Jefferies LLC, Research Division

Unknown Analyst

Yaron Benjamin Werber Cowen and Company, LLC, Research Division

Presentation

Operator

Ladies and gentlemen, thank you for standing by, and welcome to the FibroGen Third Quarter 2020 Financial Results Conference Call.

[Operator Instructions] Please be advised that today's conference call is being recorded. [Operator Instructions]

I would now like to hand the conference over to your first speaker, Mr. Michael Tung. Thank you. Please go ahead.

Michael Tung

Investor Relations Executive

Thank you, Robert, and good afternoon, everyone. I'm Michael Tung, Vice President of Corporate Strategy and Investor Relations at FibroGen. Joining me on today's call are Enrique Conterno, our Chief Executive Officer; Dr. Percy Carter, our Chief Scientific Officer; Pat Cotroneo, our Chief Financial Officer; Thane Wettig, our Chief Commercial Officer; Dr. Peony Yu, our Chief Medical Officer; Chris Chung, our Senior Vice President of China Operations; and Dr. Elias Kouchakji, our Senior Vice President of Clinical Development, Drug Safety and Pharmaco Vigilance. The format for today's call includes prepared remarks from Enrique and Pat, after which, we will open up the call for Q&A.

I would like to remind you that remarks made on today's call include forward-looking statements about FibroGen. Such statements may include, but are not limited to, our collaborations with AstraZeneca and Astellas; financial guidance; the initiation, enrollment, design, conduct and results of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities; commercial results and results of operations; risks related to our business and certain other business matters. Each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those projected in that statement. A more complete description of these and other material risks can be found in FibroGen's filings with the SEC, including our most recent Form 10-K and Form 10-Q. FibroGen does not undertake any obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

The press release reporting our financial results and business update and a webcast of today's conference call can be found on the Investors section of FibroGen's website at www.fibrogen.com.

And with that, I would like to turn the call over to Enrique Conterno, our CEO. Enrique?

Enrique A. Conterno

CEO & Director

Very good. Thank you, Mike, and good afternoon, everyone, and welcome to our third quarter 2020 earnings call.

We're making a strong progress on our commitment to bringing our potential first-in-class medicines to patients suffering from chronic and life-threatening conditions despite the challenges presented by the COVID-19 pandemic. I will begin today's call by providing a high-level summary of the most important accomplishments and developments from the last few months. Pat Cotroneo, our CFO, will then review the financials. After which, we will open up the call to your questions.

Today's call will include a high-level review of the roxadustat data from the recent American Society of Nephrology Conference, our continued strong China results and updates on roxadustat and our clinical trial programs. So let us get started with the recent ASN meeting.

This year at ASN Kidney Week, alongside our partners, AstraZeneca and Astellas, we presented new analysis on roxadustat, our investigation of first-in-class oral treatment for patients with anemia of CKD.

Together with our partners, we had 42 presentations, including 10 oral, which add to the understanding of roxadustat's efficacy and safety profile and the unmet need -- and the unmet medical need in anemia of CKD. The roxadustat clinical data demonstrated consistent efficacy and reassuring safety results across the continuum of CKD patients with anemia, adding to the established body of evidence highlighting roxadustat as a potential foundational treatment for this condition affecting millions of patients. We also presented data on the significant burden of anemia of CKD, a reminder that new treatment options for these patients are sorely needed.

On the efficacy front, a major goal in treating anemia is to reduce the risk of red blood cell transfusions, a significant risk for CKD patients. And roxadustat demonstrated a statistically significant improvement in this important clinical measure. The efficacy results were consistent across a wide range of patient populations, including non-dialysis-dependent, incident dialysis, dialysis-dependent and peritoneal dialysis, and included analysis in patients with diabetes, heart failure and systemic inflammation. Roxadustat demonstrated the ability to consistently maintain hemoglobin levels above 10 in the vast majority of patients. And data from the trial suggest that the risk of transfusion increased four to fivefold in patients with hemoglobin levels less than 10 versus those with hemoglobin levels greater than 10, regardless of treatment.

Moving to safety. Two late-breaking abstracts explored cardiovascular outcomes of patients with anemia of CKD treated with roxadustat, including the associations of MACE and MACE+ rates at various hemoglobin levels. In this post hoc analysis, patients who achieved hemoglobin levels above 10 had lower rates of MACE and MACE+ than patients who achieved hemoglobin rates below 10. Another presentation of an exploratory analysis showed a lower rate of hospitalization for heart failure in dialysis-dependent CKD patients treated with roxadustat when compared with epoetin alfa. Finally, multiple presentations reinforced roxadustat's safety profile related to neoplasm, hypertension and ophthalmological effects.

In summary, roxadustat was a highlight of the ASN conference with 20 of the top 10 viewed posters, including the top 2. We appreciated a widespread interest with the potential for roxadustat to transform the treatment of patients with anemia of CKD.

Moving now to China. In China, we're pleased to report net sales of roxadustat of \$22.7 million for the third quarter versus 15.7% in the second quarter. We're seeing an increase in uptake, which is being driven by both an expansion in hospital listings and broad adoption with enlisted hospitals.

Hospital listings continue to be a key focus of our launch efforts. Notably, as of the end of the third quarter, roxadustat was listed at hospitals representing approximately 55% of the CKD anemia market opportunity in China. This is in comparison to the 45% reported at the end of the second quarter.

We continue to see significant roxadustat utilization across the range of different patient populations with anemia of CKD. About 2/3 of patients from roxadustat are on dialysis, split between hemodialysis and peritoneal dialysis, and within hemodialysis, initial adoption has been in patients who do not respond well to ESAs as well as incident dialysis patients. This broad utilization pattern bodes well for long-term success and provides important learnings as we prepare to launch roxadustat in the U.S. and other countries. We look forward to keeping you updated as we advance our long-term goal of making roxadustat the standard of care in treating China's CKD anemia patients.

Let us turn now to the U.S. regulatory review and commercial preparation for roxadustat. We continue to be pleased with the cadence of and engagement with the FDA. And as we have discussed previously, we will not be making comments on the ongoing interactions with the FDA. We and AstraZeneca are working closely on U.S. launch preparation activities.

Assuming a positive decision by a PDUFA date of December 20, the plan is to immediately apply for the Transitional Drug Add-on Payment Adjustment or TDAPA, which would provide reimbursement for roxadustat for dialysis-dependent patients outside of the prospective payment system bundle. The earliest roxadustat could receive TDAPA coverage would be April 1, 2021. And should that occur, the official launch within the dialysis organizations would commence.

Assuming approval, roxadustat will be available in the first quarter of 2021 and we plan to officially launch in a non-dialysis-dependent setting in the second quarter of 2021. Disease awareness activities and discussions with payers are well underway. We have submitted manuscripts covering the Phase III data for publication, both for the individual trials and pooled data sets, and expect to have them at the time of launch.

Finally, we continue to work with large dialysis providers on our 2 ongoing Phase IIIb roxadustat clinical trials in the U.S. dialysis setting. In Europe, the filing for roxadustat for the treatment of anemia in adult patients with CKD, both on dialysis and not on dialysis, is under review by the European Medicines Agency. In Japan, the sNDA filing for the indication of anemia of CKD in non-dialysis-dependent patients is under review and we continue to expect the decision by year-end.

Moving now to our pipeline, I would like to provide time line guidance for our clinical trials. Please note that the COVID-19 pandemic continues to present challenges to the conduct of clinical trials across our industry, and we continue to monitor the situation and will take actions as necessary.

Starting with roxadustat. For our Phase III trial in myelodysplastic syndromes or MDS, we expect top line data in the first half of 2022. For our Phase II trial in chemotherapy-induced anemia or CIA patients, we expect top line data in the second half of 2021, and if successful, plan to quickly initiate the Phase III program.

Moving now to pamrevlumab. As we have mentioned over the prior months, the most affected of our trial continues to be pamrevlumab's ZEPHYRUS IPF trial, in which we paused enrollment due to the vulnerability of these patients with severely compromised lung function. Unfortunately, the current COVID situation continues to be extremely challenging for enrollment and has also delayed the initiation of ZEPHYRUS-2. As such, we will be providing guidance for pamrevlumab in LAPC and DMD, but not on IPF at this time. Given the different COVID scenarios, there is variability in our projected IPF enrollment time lines, and we will continue to evaluate and plan to update you at the appropriate time.

In August, we initiated LELANTOS, a Phase III trial of pamrevlumab in approximately 90 patients with non-ambulatory Duchenne muscular dystrophy or DMD. And we expect top line data in the second half of 2022. We also plan to initiate a second Phase III trial, LELANTOS-2, in approximately 70 patients with ambulatory DMD.

Finally, for LAPIS, our Phase III trial in locally advanced unresectable pancreatic cancer, we expect top line restriction data in the second half of 2022. We remain focused on accelerating enrollment of all of our ongoing clinical trials while ensuring patient safety.

Lastly, I want to welcome Kirk Christoffersen, who has just joined FibroGen as Chief Business Officer, with responsibility for business development and alliance management and reporting to me.

I will now turn the call over to Pat Cotroneo, our CFO, to review the financials. Pat?

Pat Cotroneo

Chief Financial Officer

Thank you, Enrique.

As announced today, total revenue for the third quarter of 2020 was \$44 million as compared to \$33.2 million for the third quarter of 2019. The current quarter revenue consists of net product revenues of \$22.7 million for roxadustat sales in China, \$20.7 million in development revenue, \$2.3 million for sales of bulk drug product to AstraZeneca and a net reduction of \$1.7 million for certain adjustments. For the same period, operating costs and expenses were \$11.7 million and net income was \$33 million or \$0.36 per basic and \$0.35 per diluted share as compared to operating costs and expenses of \$86 million and a net loss of \$49.4 million or \$0.57 per basic and diluted share for the third quarter last year.

As mentioned in our last quarter's call, we recently amended our China collaboration with AstraZeneca. The new agreement more optimally aligns both FibroGen and AstraZeneca to maximize the economic value

of the roxadustat franchise and will result in improved and more predictable economics and profitability for FibroGen.

Under this amendment, in September 2020, FibroGen Beijing and AstraZeneca completed the establishment of a joint distribution entity that will perform roxadustat distribution as well as conduct sales and marketing through AstraZeneca. We amended the collaboration in a number of ways, including establishing the cap on sales and marketing expenses. Historically, these co-promotion expenses were billed to FibroGen and payment was deferred until certain profitability and liquidity provisions were met. At that time of the amendment, we also settled the historical co-promotion costs for both parties to reflect an equal sharing of historical losses and made an adjustment of the co-promotion expenses. As a result of these changes, we reversed approximately \$84.4 million of co-promotion expenses, which were recorded as a reduction to selling, general and administrative expenses in the third quarter of 2020.

Once the distribution entity is fully operational, FibroGen is expected to recognize revenue based on its sales to the distribution entity, while AstraZeneca is expected to consolidate the distribution entity and recognize revenue on sales to customers. This amendment better aligns the parties' interest and is expected to enable profitability for roxadustat commercialization in China at an earlier point in time.

Included in operating costs and expenses for the quarter ended September 30, 2020, was an aggregate noncash portion totaling \$23.6 million, of which \$17.9 million was a result of stock-based compensation expense as compared to an aggregate noncash portion of \$19.6 million, of which \$14.8 million was a result of stock-based compensation expense for the same period in the prior year. At September 30, FibroGen had \$719.3 million in cash, cash equivalents, restricted time deposits, investments and receivables.

Looking ahead, we have a total of \$245 million in potential milestones expected over the next 9 months for anticipated U.S. and EU approvals and first commercial sale in the U.S. At this point in time, we have no changes in expectations in any of the anticipated milestones between now and mid-2021.

Based on our latest forecast data, we now estimate our 2020 ending cash, cash equivalents, restricted time deposits, investments and receivables to be in the range of \$770 million to \$780 million, assuming U.S. NDA approval in Q4 2020.

Thank you. And I would now like to turn the call back over to Enrique.

Enrique A. Conterno

CEO & Director

Thank you. And in summary, FibroGen is well positioned to continue to make progress in the current environment. Our business continuity plans are in effect and we're seeing some impact to operations resulting from COVID-19. We have the capabilities and resources to navigate through these uncertain times and achieve our stated goals.

As roxadustat sales ramp-up in China, our financial position is strong, with approximately \$720 million in cash at the end of the third quarter and a total of \$245 million in approval and first commercial sales milestones expected over the next 9 months. We received full partner reimbursement for all development and commercialization of roxadustat in all geographies except China, where we shared these expenses 50/50 with AstraZeneca. We have an excellent cash position with which to advance our research and development agenda and are looking forward to the roxadustat regulatory decision in the U.S. by yearend.

Robert, if you could now open the lines for questions.

Question and Answer

Operator

[Operator Instructions] We'll have our first question coming from the line of Michael Yee with Jefferies.

Michael Jonathan Yee

Jefferies LLC, Research Division

Congrats on the progress, particularly in China. I had a 2-part question. One was regarding the big picture implications of whether a drug has a black box or not. And while AstraZeneca had some very nice comments this morning, I guess, for investors, is there an implication to the opportunity? Or do they use -- I'm sure you've thought about this, whether a drug has a black box or not. So maybe just run through what those things might mean.

And then the second question relates to the ASN presentation, which you nicely summarized. And I guess, the idea that having less cardiovascular events as hemoglobin goes up seems very good, but that's, of course, how Amgen maybe got in trouble later on. What is the implication of that towards thinking about cardiovascular safety? And don't you need to show the control arms as well?

Enrique A. Conterno

CEO & Director

Very good. Thank you, Michael. And let me try to address the first question. I'll try -- we'll try to answer the second question here with Peony as well.

In terms of the box warning, there are a number of scenarios. And let me just remind everyone that we are not planning to comment or speculating on what our interactions with the FDA are right now. But there are a number of -- you can speculate about a number of potential scenarios, if you wish.

So on one side, you can take basically no box warning on -- across any of the indications. Maybe to the other end, you can say, well, we have a box warning that reads like the box warning that ESAs have. Clearly, somewhere in between, maybe a box warning that maybe reads a little bit differently than what the ESAs' box warning is.

As we think through this, clearly, when -- first, when we look at the dialysis setting, it is pretty clear that, today, I think the products that are being utilized for treatment -- and patients are treated for anemia in the dialysis setting in the vast majority, we have those products being a -- having a box warning. So in this particular setting, having a box warning, it is not a disadvantage for use, right? So clearly, not having a box warning is even better, but it's -- I view that as something very manageable given the current setting.

When it comes to NDD, we are -- in this particular setting, we have most of the patients being untreated. So it's an opportunity to basically build the market and make the case for roxadustat as a compelling value proposition to be able to treat these patients. But it's a different situation because we are trying to increase treatment rates and ensure that instead of having 1 out of every 10 patients being treated in that setting, that we can move truly the needle over time.

Clearly, in that setting, a box warning actually would slow the uptake, in particular the initial uptake as physicians get more comfortable with utilizing the product. So that's maybe some of the frame that -- I don't see longer term, when we think about the absolute addressable market, that being a huge issue, but it will slow down the uptake in the near term.

In terms of your second question on ASN, and I think you are referring to the data that we presented on achieved hemoglobin levels and corresponding MACE outcomes. Just to recap what the -- what our interpretation of this analysis say, is basically that we basically saw higher rates at hemoglobin levels below 8, very high rates of MACE. Rates of MACE decrease as hemoglobin increased. And for hemoglobin above 10, we basically saw the lowest rates of MACE and MACE+ events.

And this data was quite consistent. This pattern was quite consistent in both DD and NDD. We -- our intent of that analysis -- I think it's important data, but to me, I think the #1 interpretation of that analysis -- and let's keep in mind that this is a post hoc analysis, right? So we need to view it that way. It's just mining the data that we basically have from Phase III trials, we should do so, they are exploring -- we should view them as exploratory analysis.

But I think the #1 take is that anemia needs to be treated. And we need to treat it seriously because, clearly, what we basically see is that for low rates -- when hemoglobin is low, we basically see high rates of anemia. By the way, this -- also below 10, we saw transfusion rates increase almost four to fivefold. So it is basically -- our own interpretation is basically around treatment of anemia and the importance of doing so from a medical perspective.

Operator

Next question will be coming from the line of Jason Gerberry with Bank of America.

Unknown Analyst

This is [Fadi] on for Jason. Can you help explain the market dynamics in China? Based on data from AstraZeneca today, the patient numbers more than doubled from 40,000 to 90,000 from 2Q to 3Q, but sales -- the sales increase did not match that rise in the number of patients. Can you help explain that?

Enrique A. Conterno

CEO & Director

Yes. Let me try to provide some color on China. And then I'm going to ask Chris Chung to also help provide some additional commentary.

Clearly, we are very pleased with our China launch. We achieved reimbursement at the beginning of the year. And as of the end of Q3, we are already listed in 55% of the hospital. This is really quite extraordinary as we look at comparable launches, even of products that have become very significant products in China. So very significant listing progress, and that is key and I think it's a great signal for long-term success.

In addition to that, of course, we're seeing the adoption within those listed hospitals. And we just reported basically \$22.7 million in the Q3 versus the \$15.7 million that we reported in Q2, so good consistent progress. And when we look at the underlying business fundamentals, I consider them to be very, very strong.

Right now, I think we view that roxadustat has the potential to become what I would describe as a blockbuster in China. I would define that as a product that has revenue north of \$0.5 billion, so \$500 million. So very significant opportunity, and we're launching well to be able to try to aim towards that.

Clearly, we also see our utilization across a breadth of patients, which I think is very important as we think about long-term success. Many different opportunities for us to grow with different segments.

As it relates to your question, my understanding -- I'll ask Chris to confirm because -- but the number of patients that were reported by AstraZeneca, they were cumulative patients as opposed to the patients in the quarter. And as you know, the duration of -- there are some patients that stop treatment, some patients that stop treatment. So I don't think that we will be able to just do a calculation that we increase the number of patients and we're going to double the demand. But we're very pleased in terms of where we are and the opportunity to have roxadustat start benefiting so many patients in China.

And Chris, maybe if you could comment?

Christine L. Chung

Senior Vice President of China Operations

Sure, Enrique. So very quickly, to supplement what Enrique said, the sales we report are ex-factory sales. I think patient points more to demand sales in terms of what is actually sold to the patient -- to the

hospitals and what's actually prescribed. So I don't know that we could directly link the 2 in that linear of a manner.

As Enrique said, there's tremendous uptake, but still we're at the early launch stage where there's some new patients, new prescribers who are just getting on drug. We're trying to track the DOT as best we can, but there's a lot of variability. At this time, it's very difficult to link demand to the number of patients, but as you can see from our ex-factory sales, it's a very robust trajectory, and we remain very optimistic in terms of what this tells us about the market opportunity.

Operator

Next question will be coming from the line of Annabel Samimy with Stifel.

Annabel Eva Samimy

Stifel, Nicolaus & Company, Incorporated, Research Division

So I had a question about what you expect the launch trajectory. I know that in the dialysis population, you expect to ramp relatively quickly. Can you talk a little bit about how you expect -- or how AstraZeneca expects to build the non-dialysis population just beyond some of the reimbursement challenges or hurdles, where do you expect the primary adoption hurdles to be? Given the wealth of data that you have, it seems like physicians can understand the benefit rather quickly, notwithstanding a black box or no black box. So what are some of the considerations you're thinking about in the NDD population?

Enrique A. Conterno

CEO & Director

Yes. Clearly, the 2 settings are different and they also respond to different reimbursement mechanisms. First thing, I think, for a launch anywhere, we need to ensure that roxadustat is going to be reimbursed. So we need to work towards reimbursement in both the dialysis setting. I've commented, as part of my initial comments on our plan to submit for TDAPA, and expect that the earliest date that we could get reimbursement will be April 1, 2021.

In the case of NDD, we are also in discussion with payers. And in this particular case, I think we need to be placed in formularies, in the different formularies. So those arrangements will need to be made and we want to make sure that we are supporting AstraZeneca to be able to have those arrangements as quickly as possible. So that's an important part of thinking about just ensuring that there's going to be adequate reimbursement over time.

We need to think about -- as we think about NDD that -- in this particular case, it is not just about treating the current patients that are being treated. So we need to basically educate the overall marketplace on the importance of treating anemia. And that's why I'm insisting on the comments of some of the benefits when it comes to anemia and some of the comments that I made during the initial comments in this conference call. That is incredibly important that we are upfront. Now roxadustat has, as you mentioned, a number of benefits. So we think that it has the right efficacy safety profile to be able to have a really good uptake in the NDD setting and be able to be a catalyst for the overall expansion of that market.

We -- over time, we're not going to be satisfied with just treating 20% more patients or we need to be thinking about a scaler in terms of expanding this marketplace. And this is going to happen, of course, over time. And to do that, yes, we would need to make sure that we're reaching the appropriate physicians, not only the physicians that are prescribing and treating anemia today, but the ones that we think could -- are seeing those patients that could benefit from roxadustat. But in addition to that, we need to be thinking about patient activation, ensuring that patients understand that there is a new treatment option that is up.

So we have a great partner in AstraZeneca. And we look forward to supporting them and ensuring that we can be as successful as we can be in that setting.

I'm going to ask Thane if he has any additional comments.

Thane Wettig

Chief Commercial Officer

Yes. Thanks, Enrique. Just a couple of additional comments. When we think about the NDD market, we don't think about it as a market build. We think about it as a market rebuild just because of the number of patients who previously have been treated with an ESA that are now not being treated. And you've heard the statistics where about 1 in 7 patients in the 12 months prior to dialysis are treated with an ESA. At one point in time, it was about 1 in 3. And so our first goal will be to ensure that we can rebuild that market on the way to then, as Enrique talked about, scaling the opportunity in a much different kind of scenario as well.

And the second thing is the advantage of working with a partner like AZ is the significant presence that they have from a patient support and affordability program perspective with their internal AZ 360 hub, which we believe will be an important mechanism to ensure eligible patients have the patient support and reimbursement mechanisms in place to assist them in getting and staying on therapy.

Annabel Eva Samimy

Stifel, Nicolaus & Company, Incorporated, Research Division

Okay. Great. And if I could just follow-on one more question. You have quite a bit of cash building, that's only going to get better. You don't have a tremendous amount of expense with the launch. So is there any thought beyond just financing your R&D programs? Any additional thought to business development and things you need to build out?

Enrique A. Conterno

CEO & Director

Yes. So we're not going to be commenting on business development, but yes, that's something, as I mentioned at previous earnings calls, that after this initial phase, the first 9 months or so, which, by the way, I've been now, I think, on my job now 10 months, there will be, I think, an opportunity for us to start thinking about that and be able to think about business development and, in particular, bringing assets or signs that we believe can create significant value for patients and shareholders.

Operator

Next question will be coming from the line of Geoffrey Porges with SVB Leerink.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

A couple of quick questions. First, and I apologize if you've answered this, but what is the latest thinking on the time for the pamrevlumab pancreatic cancer study readout?

And then secondly, could you just confirm, Enrique, what you said about the launch timing for NDD and DD specifically next year, assuming success at the FDA?

And then lastly, is the data about LDL reduction meaningful to physicians and potentially helpful to launch? Or is that something that might be something that you'll be featuring?

Enrique A. Conterno

CEO & Director

Very good. Thank you, Geoff. Just let me first address your question about LAPC. When do we expect a readout? And we mentioned that we expect top line resection data in the second half of 2022.

When it comes to -- your second question was about -- or last question was about LDL and impact of LDL. We think that is a nice marker to have, but at the end, LDL is mainly utilized as a marker for cardiovascular risk. And to that extent, we have cardiovascular outcomes that, in a certain way, are comprehensive to the entire product. So yes, it's good to have the LDL data that we have, showing decreases in LDL, but I think even more importantly, it's basically to be able to showcase our overall cardiovascular safety data.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Okay. And then, sorry, just the timing, specifically for the 2 indications or populations?

Enrique A. Conterno

CEO & Director

Yes. And in terms of launch for the 2, for both DD and NDD, when we are determining the official launch, right, because clearly we expect to make the product available as soon as we can after approval, but we expect that the earliest that we would get TDAPA approval would be April 1, 2021. So that's basically what we're targeting the official launch, given that's really what would be the catalyst for the dialysis organizations to incorporate their products or using the product in the way that they -- we think they could. When it comes to NDD, we expect that the official launch would be also in the second quarter of 2021.

Operator

Next question will be coming from the line of Yaron Werber with Cowen.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

So I have a couple of questions, Enrique. One is basically a follow-up to what you just saw -- were highlighting. With Fresenius and DaVita, these better than -- are big clinics and they have pathways, and they typically will run pilot programs before they adopt a new drug. I know you've commenced a couple of studies and you're enrolling those studies in those sites. Can you give us an update on that? And how long do you think before you have data? And is it sort of a pseudo or an official pilot program?

And then secondly, on TDAPA, when we look historically at some of the drugs, whether [the irons], and you can argue they're not that innovative, or even Parsabiv, and you can argue Sensipar was out, but launches in dialysis have been pretty slow. And the profit incentive under TDAPA, really it's a small and mid-cap -- mid-chain dialysis providers that typically adopted, but not the big ones. Why would it be different with roxa?

Enrique A. Conterno

CEO & Director

Yes. I'm going to ask Peony to comment on our Phase IIIb studies, which we are conducting with dialysis organizations. Peony, would you like to make some comments?

K. Peony Yu

Chief Medical Officer

Yes. Thanks, Enrique. Yes, we are working with some of the largest dialysis organizations. And the 2 studies are going exceptionally well. This is a an opportunity for the U.S. dialysis organizations to further study our product. And the studies are expected to be finished in the first half of 2021 and will be in time to support our launch.

Enrique A. Conterno

CEO & Director

And in terms of -- thank you, Peony. And in terms of TDAPA, if I understood your question, you're looking at other examples. I will share what my view is here. But having reimbursement doesn't mean that you're going to get use, right? The reason why we believe roxadustat will be utilized is because of the overall clinical profile that it offers, not because it has a favorable -- necessarily a favorable reimbursement scheme.

So we think that roxadustat offers a number of benefits. I think if we think about straight off the bat, in incident dialysis, the excellent data that we have with -- showing basically reduced cardiovascular outcomes in this population, so that's extremely important. Clearly, there are a number of patients, we

estimate maybe about 20% of patients on dialysis, that do not respond well to ESAs or are in very, very high doses in many cases. We think those are also patients that would be -- given the experience that we have in China, we see patients that would be candidates for roxadustat right away. So to us, I think it's the overall benefit -- risk-benefit profile that the product offers.

TDAPA, in itself, I think is important because it allows for the product to be used and to ensure that there's not going to be a negative incentive or a negative economic driver. So if anything, I think it's a positive driver from a reimbursement perspective for the use of the product. So I would look not to TDAPA, but really to the profile of the product to see why we believe that product will be utilized.

Operator

Next question will be coming from the line of Difei Yang with Mizuho.

Alexandre N. Bouilloux

Mizuho Securities USA LLC, Research Division

This is Alex on for Difei. First one, I guess, given that you will be potentially first to market in dialysis, could you give us a bit of color on how you're engaging with the large dialysis providers in the U.S.? And if you would expect to secure contracts with the 2 large providers following approval? Or would you expect to secure contracts maybe in a more staggered manner or just with one of them? And then I have a follow-up.

Enrique A. Conterno

CEO & Director

Yes. Clearly, we want our -- the utilization of the product to be broad. We're not going to be commenting on where are we on our discussions with the different providers. Clearly, we need to make sure that the product will receive approval, but it is pretty clear that we've been working with them pretty closely for quite some time. Keep in mind that we conducted our Phase III clinical trials with them. We are also conducting this IIIb -- Phase IIIb studies with the dialysis organizations. So I feel that we are in a really good position. And also, what is the overall profile of, once again, the medicine that we're offering. And we think that it can be of significant value from a medical perspective so -- to patients and to health care organizations. So we feel good in terms of where we are, I think, in our discussions.

Our intent is not to -- is to try to offer the product to -- and be able to reach as many patients as we can. And clearly, getting TDAPA being effective will be critical towards that goal.

Alexandre N. Bouilloux

Mizuho Securities USA LLC, Research Division

Okay. Great. And then just a quick follow-up, another question on China. I'm wondering if you could provide a bit of color around roxa's uptake, specifically in stable dialysis patients who are already on ESAs. Are you seeing a bit more conversion to roxa from these patients today versus compared to, let's say, 6 months ago?

Enrique A. Conterno

CEO & Director

Yes. I'm going to ask Chris to maybe provide some comments on that.

Christine L. Chung

Senior Vice President of China Operations

So the way we look at the maintenance dialysis market, first of all, is those with controlled hemoglobin levels and uncontrolled hemoglobin levels and also peritoneal dialysis and hemodialysis.

So first of all, we look at the PD population. We've done extremely well in the PD population. It speaks well to the clinical profile of roxadustat. The oral administration feature obviously is additive and attractive to this population for very obvious reasons. So we're doing particularly well in PD.

In terms of HD, there is a very different value proposition for those with uncontrolled hypertension -uncontrolled hemoglobin and controlled. For those that are uncontrolled, really is the initial adoption
population and a target launch population. It speaks very well to the differentiation based on eye
mobilization and inflammation. So the clinical value proposition there is very, very strong, and that's
where we see a lot of the early adopters.

We are seeing migration into the controlled population, and the thesis there is it's important to treat. It's important to treat the target. It's important to maintain so that there's very little low variability. But as a matter of pricing, we are higher than ESA. So the value proposition and the differentiation there is a little bit different, but we're very happy to see migration into that population, which frankly was not the initial focus, but with the maturing launch, we're seeing adoption. So we're delighted to see that.

Enrique A. Conterno

CEO & Director

The last thing that I would say, and you did not ask this question, but clearly, in addition to looking at the stable patients on dialysis, clearly, I think, what we see is really good adoption within the incident dialysis patients, which, at the end, I think, is a great predictor of what the brand could be in the future.

Operator

We have our final question coming from the line of Joel Beatty with Citi.

Joel Lawrence Beatty

Citigroup Inc., Research Division

At ASN, Akebia presented data for vadadustat on their non-dialysis patients, showing that the U.S. MACE looks quite a bit better and it was the ex-U.S. MACE that was really hurting their MACE outcome. I guess, with that in mind, could you characterize how your non-dialysis data looks in terms of any differences between the MACE in the U.S. patients versus patients enrolled ex-U.S.?

Enrique A. Conterno

CEO & Director

Yes. Maybe let me just make some overarching comments because, clearly, our trial is designed a little bit different from vada in terms of we were going, as you know, relative to placebo. But importantly also, we treated 11 plus/minus 1, whether it was in the U.S. and/or OUS. So we did not -- we utilized the same treatment targets for roxadustat.

Now when it comes to roxa, I think what's important is when -- first, when we look at the overall trial, we basically see that in NDD, we were comparable to placebo. So that's when it comes to MACE. So that's critically important. We showed non-inferiority.

The best trial for us to look at, which is not part of our post study, but the first -- the best trial that will be more -- most comparable to the Akebia trials would be DOLOMITES, which is a trial where we compared against an active comparison in darbepoetin, and it was conducted outside of the U.S. So that's -- you're hitting on both points. And the hazard ratio that we saw -- and by the way, we treated to, once again, 11 plus/minus 1, okay? We saw hazard ratio in MACE of 0.81. So honestly, we feel very good about our data.

And I don't know, Peony, if you want to add anything else to that.

K. Peony Yu

Chief Medical Officer

Yes. Thanks, Enrique. Yes, we -- so that -- as Enrique said, that the DOLOMITES study is 100% ex-U.S. and we had a very reassuring hazard ratio. And now in our -- in the placebo control, which is our main program, we saw consistency in the U.S. data with -- that is consistent with the overall MACE program. So we've -- and as you know, that placebo is a high standard for a measurement of safety. And we are glad that we have chosen this standard.

Joel Lawrence Beatty

Citigroup Inc., Research Division

Maybe one other question is also on the competitive landscape. And I think recently on clinicaltrials.gov, GSK moved sooner the time lines for the readouts for daprodustat. It looks like November 2020 for dialysis and April 2021 for non-dialysis. Any predictions there for how the results could look, whether they could resemble your data? Or are there differences to consider?

Enrique A. Conterno

CEO & Director

I think that's a good question for them.

Operator

All right. We don't have any more questions on the line. Speakers, please continue.

Enrique A. Conterno

CEO & Director

Very good. Once again, I appreciate everyone's time today as we report our third quarter results.

We're very pleased with the progress, as I mentioned, across a number of fronts. And of course, we are looking forward to the action date of December 20 for roxadustat, which is the roxadustat PDUFA date here in the United States.

Thank you very much.

Operator

And this concludes today's conference call. Thank you, everyone, for your participation, and you may now disconnect. Have a good day.

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EXHIBIT HH

Company Name: FibroGen, Inc. (FGEN) Event: Stifel Virtual Healthcare Conference

Date: November 17, 2020

<< Annabel Samimy, Analyst, Stifel>>

Hi. Good afternoon. And welcome to the FibroGen Presentation. I'm Annabel Samimy, Biopharmaceutical Analyst here at Stifel. And it's our pleasure to have Enrique Conterno with us today CEO from FibroGen. So, you all are reaching a pretty critical juncture here as we approach the PDUFA date for roxadustat in December. So, all the attention is clearly turning to approval and label and of course commercialization.

So, Enrique, why don't you just give us a quick overview of where we are, and I'll just launch into Q&A.

<< Enrique Conterno, Chief Executive Officer>>

Very good, yes. So, thank you, Annabel for the invitation. We're clearly very excited as the PDUFA date approaches. Let me make some general comments about the company, because I know we will discuss a lot about roxadustat, but clearly that's in everyone's attention, I'm very excited about that. But in addition to roxadustat and our progress there, we of course have pamrevlumab, which we are pursuing in three indications in Phase 3 now in IPF, in DMD and also in locally advanced pancreatic cancer.

So, I'm very excited about the opportunities with that specific product. As we've mentioned, I think, we are making good progress in enrollment when it comes to LAPC, of course, DMD just started, but we had some challenges when it comes to IPF because of the COVID situation and those patients being particularly vulnerable. Outside of the two specific programs, roxa and pam, we also have made – we're making significant investments in research as we think about bringing the next generation of products into the clinic. We hired Percy Carter and he's our Chief Scientific Officer and I'm pretty excited about the progress and the plans that he has to make sure that we can have a research engine that has a sustainable output from a program perspective into the clinic. So, excited to be here at FibroGen, it is an exciting time for us. Annabel, we're not hearing you.

<< Annabel Samimy, Analyst, Stifel>>

Okay, great. Can you hear me now?

<< Enrique Conterno, Chief Executive Officer>>

Yes.

<< Annabel Samimy, Analyst, Stifel>>

Okay, great. Sorry about that. So, just as you rightly noted we are going to be spending a lot of time on roxadustat. So why don't I just launch into that? So not wanting to put

cart before the horse here, we do need approval for the product. I think The Street by now has accepted there'll be no AdCom. I still get the question. It's a disease area that's obviously been fraught with a lot of post-approval safety issues with a new class. So just help us understand that with — what the FDA's reasoning here was for no FDA panel. I imagine they want to cover their bases, but just their comfort level with this space maybe is what got them there. So why don't you provide us some color around that?

<< Enrique Conterno, Chief Executive Officer>>

Sure. So, clearly, I can't speculate over why the FDA has not decided to have an AdCom or call an AdCom in this particular case. As I think mentioned in the past, I think, the FDA tends to have an AdCom whenever they feel that they don't have all the adequate internal expertise, so they can get significant benefits from external advice and for either approval reasons or labeling reasons, or looking at certain subpopulations and so forth. I typically think of theAdCom, it's just part of the process of the FDA approval. I don't see it as a negative or a positive in any way. And of course, given the chance of an AdCom, we have to prepare for one and – but that's really water under the bridge.

So at this stage, I think what I can say is basically we have to rely on the data that we've shared and I feel that the data that we shared, I think is very compelling when it comes to roxadustat and the ability to basically show yes, improving, correcting and maintaining hemoglobin levels, but importantly, as a result, decreasing the number of transfusions and then the broad safety data that we have first in NDD, where we look at both our safety data there when we compared to ESAs. As you know, we have had pretty compelling data when it comes to incident dialysis we had stat sig in terms of a reduction in the number of MACE events in that setting.

And then when we look at NDD, we were compared to placebo and we basically look at comparability when it comes to overall safety. So, we feel very good about the overall package that we had. We had an incredible presence at ASN, and maybe we can talk a little bit about that, but we had 42 abstracts between us, together with our partners, AstraZeneca and Astellas at ASN, so 42 presentations in total. And we had out of the 100 most viewed posters, 20 were roxa posters and the top two. So, I think that tells you a bit about, I think, the interest by the community, but also are pretty broad scientific presence in that same.

<< Annabel Samimy, Analyst, Stifel>>

Yes, that's great color. Thank you. So, everyone now is just waiting for labels and warnings and approval. So just before I start getting into some of the nuances there, there have been several delays related to FDA inspections recently because of travel restrictions and COVID. Are you aware of any at this point? Do you have specific manufacturing inspections that have to be conducted, have been conducted or have not been conducted? Can you give us any comfort around that?

<< Enrique Conterno, Chief Executive Officer>>

Yes, I don't know if I can give you a lot of comfort in terms of giving you the color, but I can provide some context. Keep in mind that the given – that we had shared that we're not providing color on our interactions with the FDA at this stage and their labeling or manufacturing or anything like that till basically the action date. I think the context that we'll provide when it comes to manufacturing in particular, clearly the FDA has issued guidelines when it comes to manufacturing inspection during this COVID time and how they're thinking about that and the use of virtual inspections.

But clearly, I think the context that I will provide is a context of the difference between large molecules or complex biologics and small molecules. So it's a pretty big difference from a manufacturing perspective. And then also what is the track record, right, of the manufacturing sites when it comes to FDA and passing inspections and so forth. I think all of those things will play a role in how the FDA thinks about that. I think what I can share is that we feel very good about our partners that are conducting the manufacturing and about the overall submission that we've made to the FDA. So we continue to feel very confident.

<< Annabel Samimy, Analyst, Stifel>>

Okay, great. And maybe then – since, again, you're not talking about labeling and specifics there. Maybe what you could do is, I guess, give us the range – you'd given us the range actually before, are there no black box warning to black box warning and a whole range in between. But maybe you can help us to understand the impact of what you think are sort of like the extremes in the middle in terms of how that might affect your commercial opportunity.

<< Enrique Conterno, Chief Executive Officer>>

Yes. So – you're right. We've provided that those bookends. So, on one side no box warning, on the other end basically a box warning that looks like an ESA box warning. And there are a number of things in between, including, of course, with the languaging of, if there were to be a box warning, what it says as one of those in between scenarios. The way that I think about this is in two fronts. Clearly in the dialysis setting, I think what we have to always remember, those patients are already being treated for anemia for the most part. So at the end, I think, there's a choice between using what they're using today and basically a new treatment option in the case of roxadustat and what does that treatment option really offers. But the option that they're using today actually has a box warning.

So in that setting I feel that is going to be the totality of our data that basically will matter. And quite frankly I think the discussions that we have with the dialysis organizations, because in many cases, those protocol decisions are being made centrally as we – as they think about treating patients within each of the respective sites. So my sense in that case from a commercial perspective, it's really how do we fair relative to ESAs when it comes to the label itself and what advantages do we offer keep in mind that we actually – in our trial we actually showed a statistically significant higher levels of hemoglobin with our product relative to ESAs and, as I shared, a number of other benefits, but also less transfusions when we looked at pooled analysis. And finally the incident dialysis data, we think is very important when those patient's initiate dialysis. So, clearly, we have important data.

When it comes to NDD, I do think that the case that we have to make, I think, is a little bit different because in this particular case, patients are not being treated. We estimate that less than 10% of patients get treated in this setting. In fact, when you look at the last 12 months prior to dialysis, only about 14% of patients have actually received the ESA as a treatment. So the opportunity here is to significantly scale the number of patients that are actually being treated in this setting. And the opportunity is very significant. It's a very significant opportunity that will develop over time, but in a way we're building a market, so we need to increase treatment rates.

To that end, I think, it is not enough for us to think about how do we compare to ESAs, but in this particular case, the label tends to matter, in my view, more than in the dialysis setting, because we need to make that case to patients and to physicians. I feel very good about our opportunity with the data that we have to be able to build a considerable – to be able to realize the considerable opportunity that I see in that particular setting.

<< Annabel Samimy, Analyst, Stifel>>

Okay, great. And so maybe we can talk a little bit about the experience in China then because I guess the question is whether you can look at the experience there and apply it to the U.S. Clearly, there are differences between the markets, the reimbursement is different, but maybe, what about the treatment approaches to anemia and the patient type? What kind of parallels can we draw between what's happening in China versus what you think you can do here in terms of the launch?

<< Enrique Conterno, Chief Executive Officer>>

Yes, I think, it's fair to say, and I don't use this word too often, but I would say that our China launch right now I'll qualify it as exceptional when we look at what the product has achieved so far. Keep in mind that three quarters, post reimbursement, Q3 we had nearly \$23 million in net sales for the product after \$5 million in Q1 and \$15 million plus in Q2, so very significant important ramp up quarter-on-quarter. Importantly, I think, we have achieved significant listings in hospitals. Today when you look at our overall listing, we are now listed in hospital that basically represent us as of the end of Q3, 55% of the overall China market that used to take products years to be able to achieve that level of listing in China.

And I think to your question of what type of read-through can we see based on China to the U.S.? And clearly, the reimbursement is different. We have now national reimbursement in China. We're listed in 55% of the market. In the U.S., we will need to work through the TDAPA and then formularies in the NDD setting. But when I think about China in particular, what we learn is the physician adoption that we've seen in the hospital, that we are listed in is very significant, which is driving that demand and that revenue that I just spoke of.

And importantly, we see basically utilization across a number of different settings, which is very important that people see the benefit of the product, not just in one particular setting that which would be unlimiting for future growth, but basically we are growing and we are penetrating a number of different settings. About one third of our sales were NDD in China or our patients about two thirds were basically in the DD

setting. That's expected the DD uptake would be quicker, but we expect the NDD opportunity actually to be larger over time as we develop that in China as well. And then with NDD, basically different types of patients, we see peritoneal dialysis patients. We see the typical patients in the dialysis centers. So, we basically see opportunity to grow in a number of different ways, many different levers for us to grow, many different opportunities for us to grow longer-term, which I think is excellent.

<< Annabel Samimy, Analyst, Stifel>>

Okay. And then if you can, maybe qualify the usage in the NDD in China a little bit. In terms of the real-world practice, what are they finding in those patients? Are physicians gaining comfort around the safety? Are they seeing some of the clinical benefits of the anemia control? Are they getting ancillary benefits? Have you been able to draw any of that kind of data from the Chinese population?

<< Enrique Conterno, Chief Executive Officer>>

Yes, I think, what we have right now is a lot of what I'm going to call the feedback from physician, but it's more anecdotal than formal feedback. I think we need to wait a little bit to get a better data on – okay, at the end of the day how are patients faring and what are the treatment patterns, what is the overall adherence that we're basically seeing. So we need to see a little more longitudinal data to be able to comment more on that. Clearly, the feedback is very positive.

And that's one of the reasons why we see basically some of the uptake when it comes to demand and so forth across the different patient populations, but we need to wait a little bit more to look at that. Some of the feedback that we basically see is not unexpected, right. Clearly, physicians that are using the product are quite familiar with the data, not just the China data on the label, but the overall data, and what's presented in different scientific forums. But importantly, I think, clearly the ease of use of the product is something that they comment quite a bit on.

And of course, that's expected. That's not how I would hang my hat on, I would want to make sure that at the end, people are looking at all of the better outcomes that we can develop, right? The fact that people have better hemoglobin control and therefore they can reduce the risk of transfusions. And we hear that, we hear how quickly people can correct their hemoglobin and the efficacy of the product. So we have — we do a lot of market research and that's something that really stands out, which is we just have an excellent benefit risk profile that the product offers.

<< Annabel Samimy, Analyst, Stifel>>

Okay. And you don't know at this point how long on average patients are able to stay on treatment?

<< Enrique Conterno, Chief Executive Officer>>

We do have some initial data, but I think, it's important that we wait a little bit long. It's still relatively early, I think, in the life cycle to be able to look at that. And so it is likely we will comment on that at the start of the New Year.

<< Annabel Samimy, Analyst, Stifel>>

Okay. All right. Great. And then anything that would be done differently in the U.S. market – outside of like the reimbursement landscape being very different, anything that you would – that you learned from the Chinese launch, that AstraZeneca learned from the Chinese launch to bring over to the U.S. to make it more effective or optimize it in any way?

<< Enrique Conterno, Chief Executive Officer>>

Well a few things, but clearly, I think, one of the surprises in China is how quickly we've been able to realize or start to realize the opportunity will be in NDD. We thought that would take longer. So I think that's a great aspect for us to think about. And that opportunity is very important and we – let's make sure that we go after that opportunity, not just thinking about the long-term, but also what is that we could build with that opportunity quickly.

As you know, it is – given the data that we have ahead of our competitors, it is likely that we – yes, we have to build this market, but we're also going to be there as the sole – likely the sole HIF PHI for a number of years. Andit's an incredible opportunity that I want to make sure that we maximize.

<< Annabel Samimy, Analyst, Stifel>>

Okay. All right, great. So why don't we talk about the uptake in the DD market, obviously that can go relatively quickly, not only because you are offering a better alternative to ESAs. But also because you've got a concentration of the customer base. So you're negotiating probably at a corporate level with – in a negotiation with two players, essentially you can get 68%, 70%, 80% of the market, frankly. So just help us with the logistics there and what can we think of a ramp-up realizing very well that you need the TDAPA payments, could you realize sales before you actually get that TDAPA payment or is it just, first quarter is a wash and then we should just assume sales after that?

<< Enrique Conterno, Chief Executive Officer>>

Yes, I think I have to start there with basically the overall clinical profile of the product and what it could offer the dialysis organization. So we feel very good about our data. Keep in mind that we worked with those dialysis organizations in our Phase 3 trial. So they are already knowledgeable to a certain degree of the product. But also we are conducting with dialysis organizations 3b studies now as we speak.

And then as you will point out, typically they basically implement certain standards and protocols in the dialysis settings. So those discussions tend to happen at the corporate level. And AstraZeneca is the one leading some of those discussions with the dialysis organizations. And clearly it is about the clinical profile, it is what roxa can add. And there's no question those discussions are important.

And of course TDAPA plays a critically important role because TDAPA allows basically for the product to be added into those settings without being included to the bundle, which would make it significantly more difficult. We expect that roxadustat will be eligible for the TDAPA, and we've shared that we expect that inclusion will happen as early as basically April 1 of next year, the inclusion of TDAPA. TDAPA is a huge catalyst, I think, for the product. And you are right, I think, with the inclusion of TDAPA, I think, what we expect is that uptake and utilization can be very fast.

<< Annabel Samimy, Analyst, Stifel>>

So is there anything – so I think if I remember correctly, CMS, said that all NCE starting January 1 of 2020 would get automatic TDAPA payment. I imagine that roxadustat is an NCE, so does it fall into that category automatically, or do you have to still apply for it and wait for it?

<< Enrique Conterno, Chief Executive Officer>>

Now, you still have to apply and you still have to wait. So you basically make an application for TDAPA. You need to get a code as well, but only now you basically that submission to CMS. CMS needs to review that, and then your eligibility basically happens – should happen basically at the start of the next quarter, right? In this particular case, given our approval is – our PDUFA date is December 20, we basically believe that it is reasonable for us to think about that we could get – we will get that and we could get that would be April 1. So part of the discussion that we had with CMS, we have – we believe that roxadustat will be eligible.

<< Annabel Samimy, Analyst, Stifel>>

Okay. Now, going back to your other comment with regard to some piloting that the dialysis providers are conducting right now, they've obviously worked within clinical programs with roxadustat. What are they going to be learning from the piloting of this product to gain additional experience, to get them comfortable? Are there certain metrics that they're looking for? Is it economic metrics? Is it healthcare outcome measures? What are they looking to learn from this piloting?

<< Enrique Conterno, Chief Executive Officer>>

Yes. Keep in mind; whenever we conduct the Phase 3 trials, we are looking at the product from the perspective of evaluating the efficacy and the safety of the product from that perspective of FibroGen. Clearly, we've already said and have demonstrated both the efficacy and the safety of the product. So, when it comes to the Phase 3 studies we are now working within each of the dialysis organizations to better assess basically this product within those specific settings, right.

So, we're working with them to basically structure these studies to make sure that the data that we get from these studies is meaningful, not just in a broad sense to roxadustat, but meaningful to the specific dialysis organizations.

So, I'm not at liberty to disclose everything that we're looking at, but we've, of course, worked very closely with them to ensure that these trials meet their needs. And it's a

great opportunity you call it a pilot and it's really a Phase 3b study, but clearly in a certain way, it's a way for them to think about also, okay, how does roxadustat work within those settings and get the advanced learning from that?

<< Annabel Samimy, Analyst, Stifel>>

Okay. Will they be releasing that data at any point?

<< Enrique Conterno, Chief Executive Officer>>

Well, I think, the expectation is yes. We expected to conclude those trials early – in the first half of next year. And at some point in time, we will intend to disclose all of that data as well.

<< Annabel Samimy, Analyst, Stifel>>

Okay. Then if we can move to NDD for a moment, what kind of conversations have you had with payors ahead of approval? And how long do you expect it to take to get these – the drug incorporated into the various plans? Is it your standard six-month wait until everyone sort of gets on-board with it, or do you think this is a drug that's in pretty meaningful demand for this population given there's really nothing adequate for them with the assay ESA?

<< Enrique Conterno, Chief Executive Officer>>

Yes, I think the aim is to ensure that patients can have access to the product as soon as possible, all right. To achieve that there are a number of things that that we need to look at. But let's keep in mind, it is AstraZeneca really that is conducting those negotiations with the payors. Clearly, I think the key is going to be to ensure that we have the discussions with the payors to ensure that we can include this product in the formularies as soon as possible. And even if it's not included immediately in the formularies, ensure that there's no exclusion for the utilization of this product, but it can still be used.

So we are in the process of working with all these organizations. As you know, I think, if we were to go back maybe eight to ten years, formulary [indiscernible] (0:27:19) used to happen once a year, now they happen much more frequently. There are meaningful updates in commercial formularies and other types of formularies every quarter. So we want to take advantage of that, and I think, that's something that we look forward to executing.

Typically, when it comes to Part D, Part D tends to basically – the formularies are set in advance and they typically happen once a year. And the submission to CMS actually happens pretty early. So, the submission for 2021 already happened in May, right. So in May we'll do our submission for 2022. But that doesn't mean that the product cannot be covered. There are a number of things that we are working on to try to think about how can we ensure that at the end of the day the patients can have access to this product.

<< Annabel Samimy, Analyst, Stifel>>

Okay. And what part of the market is Medicare Medicaid? In terms of the NDD population, I know a lot of it is commercial, but what percent of that...

<< Enrique Conterno, Chief Executive Officer>>

When we think about NDD north of 50% will be Medicare, commercial maybe a little bit over 30%, Medicaid maybe about 10%. I don't have the numbers in front of me, but those seem like the right numbers.

<< Annabel Samimy, Analyst, Stifel>>

Okay. All right. Great. And maybe you can just talk about the market opportunity in terms of, initially going after first in patients who had been treated before who've dropped ESAs and now would be eligible to be treated again. That's the low-hanging fruit sure, but there's clearly a portion of the market that still chronically anemic. So what part of that – what portion of that market is chronically anemic that should be treated?

<< Enrique Conterno, Chief Executive Officer>>

Yes, I think when we think about this market we shouldn't be thinking about what it is today, what the status quo is today, when we think about NDD, or really given what it was maybe six or 10 years ago when the market was significantly larger. We need to be thinking about establishing a new standard of care for anemia and patients within NDD.

The question is, how do we go about doing that? And clearly there is an element of the offering, so what does the product offers. Making sure that physicians feel comfortable with the product because of the – when we think about the physician community that are going to be largely treating many of these patients and the fact that in many cases some of these physicians would also have already experienced in the DD setting, my sense is that is going to inform, can be a pretty good catalyst and inform the NDD setting as well in the case of nephrologists.

So what I expect is for that education to be able to happen relatively fast. And then I think we need to make sure that patients are aware of this product and this alternative. So we will need to somehow find a way to activate patients, so they know that there's an alternative out there. And at the end, anybody that is basically suffering from anemia should be treated to make sure that they can realize the benefits of this product.

I think on your question, how large is this market? It is very significant. I think it's enough to say that while initially we see just like in China, DD maybe having more patients in DD. Over time, I believe, that the opportunity in the NDD setting actually dwarfs the opportunity in the DD setting. We look at the number of patients, longer term what this could mean for the number of patients being treated, benefiting as a result the revenues for roxadustat.

<< Annabel Samimy, Analyst, Stifel>>

Okay. We're going to do rapid-fire in the last moment. When do we expect data from the chemotherapy induced anemia? When do we expect data for MDS? And is there any additional data we should expect from Pamrevlumab in COVID?

<< Enrique Conterno, Chief Executive Officer>>

Yes. I think in the case of chemo-induced anemia, as you know, we have a Phase 2 trial that is ongoing. We should have data in the second half of – a readout in the second half of next year. And our intent will be to initiate the Phase 3 trial after that. In the case of MDS, it is a Phase 3 trial. We expect data in 2022, and that's what we've shared. So those are the two key trials when it comes to additional potential indication for roxadustat.

As you know, the chemo-induced anemia indication is very significant, given what we saw in the past with ESAs. So when you look at the number of patients that could benefit, it's very, very significant. And also the doses tend to be higher; at least the ESA doses for those patients were higher. So made that a very, very significant sizable opportunity. What was your last question?

<< Annabel Samimy, Analyst, Stifel>>

Any expectation around pamrevlumab in COVID or should we not be factoring that into our calculations at all at this point?

<< Enrique Conterno, Chief Executive Officer>>

Yes, those trials are ongoing. And given the search in COVID clearly those trials are enrolling better in particular, the trial in Italy and so forth. But clearly, I think, we view, I think, the COVID opportunities differently than we view the three indication that we have in Phase 3. So we have three indications in Phase 3 in IPF, DMD, and LAPC. Because those indications, each one of them, I think, is very significant on its own. And we have data already Phase 2 data. When it comes to COVID really, we have an intent, we have an aim, but this is the first data that we'll be generating in that space. And by the way, there's a lot of competition right now in COVID.

<< Annabel Samimy, Analyst, Stifel>>

Yes. Okay. Great. Well, we are out of time. And I was trying to get everything in there as much as I possibly could. But I think we've covered most of it. And I guess we'll have to do another one of these one day to get more questions in there.

<< Enrique Conterno, Chief Executive Officer>>

Very good. Thank you very much, Annabel.

<< Annabel Samimy, Analyst, Stifel>>

Thank you very much. And good luck with the rest of your meetings.

<< Enrique Conterno, Chief Executive Officer>>

Thank you.

EXHIBIT II

S&P Global
Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Thursday, November 19, 2020 5:35 PM GMT

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Call Participants

EXECUTIVES

Enrique A. Conterno *CEO & Director*

ANALYSTS

Michael Jonathan Yee Jefferies LLC, Research Division

Presentation

Michael Jonathan Yee

Jefferies LLC, Research Division

Hello, everyone, and welcome to another great session at the Jefferies Virtual Global Healthcare Conference in London. I am doing this fireside chat from London bridge is here behind me. And Enrique, my good friend at FibroGen, Chief Executive Officer, Enrique Conterno, is there at the headquarters in San Francisco, hard at work in bringing forward roxadustat.

I just wanted to turn it over to Enrique and maybe take a step back and ask you an important year, this year, of course, culminated with the potential PDUFA date and then even more important 2021 as you go out and try and execute on a commercial launch.

Question and Answer

Michael Jonathan Yee

Jefferies LLC, Research Division

So I wanted to start by asking you, what are you most focused on here, as we get into the end of the year, certainly, regulatory discussions is one of them. How are you thinking about the evolution of the regulatory discussions and the results, and how you're thinking about preparing for 2021?

Enrique A. Conterno

CEO & Director

Well, first, Michael, great to see you, and thank you very much for the invitation. This is no doubt a very exciting time for FibroGen with the PDUFA date coming up quickly. Now there's a lot of attention, of course, on roxadustat. But not just the regulatory process, but also the commercial preparations in the U.S. because we want to make sure that we can have an outstanding launch.

Now you asked about the broader priorities, but clearly, roxadustat is also being developed in 2 additional indications, MDS, in Phase III and CIA in Phase II. We expect beta for CIA in the second half of next year, likely maybe spilling into the first half. So that's also pretty exciting. And clearly, we have the China launch, which is, I would describe it as going extremely well.

Moving to our second important asset is pamrevlumab Phase III studies, very much focused on execution on this important indications of high unmet needs in IPF, DMD and LAPC.

So important work that we're doing, and we can have a discussion. And finally, I think something that we have not discussed a lot, but we are quite focused right now on reenergizing our research efforts. And I'm very excited about some of the progress that I see us, how we're thinking about it, as you know, we brought in a new Chief Scientific Officer, Percy Carter and excited that he's leading those efforts.

Michael Jonathan Yee

Jefferies LLC, Research Division

Fantastic. Well, I can't wait till you tease us with a new compound.

Enrique A. Conterno

CEO & Director

Yes, very good.

Michael Jonathan Yee

Jefferies LLC, Research Division

Very good. All right. Well, before we get to talk about that, we need to make sure you execute on roxadustat first. I don't want to get into the details specifically about the interactions. My question ultimately is, as you get here towards the end of the PDUFA, what -- or how will you help investors out, thinking about the 2 or 3 different scenarios.

One of those scenarios is approval with a clean, very, very, very clean broad label. One of those scenarios is approval, but maybe it looks a little more like an EPO label and one of them could be a delay. Things happen. It's COVID, I'm not sure. But talk about those different scenarios. And what are the implications of each one of those?

Enrique A. Conterno

CEO & Director

Yes. Clearly, we have a high level of conviction on the overall submission, the strength of our data, so what I'm going to focus on is basically thinking about really the bookends of maybe what the label

will look like. And on one hand, I think you have a label -- and I know there's a lot of focus on the box warning, but our label that doesn't have a box warning.

On the other hand, you have basically, on the other bookend, a label that has a box warning that looks like the EPO box warning. There are, of course, a number of scenarios in between. The wording of the box -- of a potential box warning would be important, including what populations are included in that box warning. So clearly, I'm unable to comment on our current interactions with the FDA, but I think the cadence is good. And we expect, quite frankly, approval by the -- or an action by the PDUFA date.

Michael Jonathan Yee

Jefferies LLC, Research Division

Can I -- that's really important. That's great. And I think that's helpful because actually, I've gotten a lot of investor questions about how it may not just be as simple as black box or no black box. Are you implying that if you go look at different classes, different black boxes, say different things, you could actually have comments in a black box only on a specific indication, but on a different indication because I've actually never really seen that. But help me out, now those -- all those are different things. So I need to -- if there is one. I need to read it and then look at that?

Enrique A. Conterno

CEO & Director

Yes. I think we need to wait, of course, for our particular scenario. I'm not implying that we will have that, but all of those are possibilities. Clearly, I think the -- when we look at our data, we continue to feel that the data basically offers a very favorable risk-benefit profile for patients across the continuum.

Now one comment on any details at this stage. But yes, I think key is going to be for us, for us to look at the entire label, if there is a box warning, and that needs to be put into the context.

And what is the rest of the label also say. So we of course, as you can imagine, we think about all scenarios from a planning perspective, and now we're prepared for all scenarios and prepared to execute.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. So let me talk about, regardless of what the label says, we have to go about and launch. And can you remind us in the United States first, since this is the country we're talking about. Who takes the lead? Is it -- how does it work? What are your economics? What is your involvement in the things? First of all, talk about that first.

Enrique A. Conterno

CEO & Director

Sure. So clearly, we have a great partner in AstraZeneca that has taken the lead in the United States. FibroGen, I think contributes to the launch efforts in the U.S., with the things that we can do well, which is, of course, providing the rationale behind the science and medical affairs.

So for example, when it comes to publications and when it comes to running the Phase IIIb studies, right now, with the LDOs those are things that FibroGen has taken the lead on. So we are excited about our preparations.

As you mentioned, I think the economics for FibroGen, we do not -- outside of China, we are fully reimbursed for all of our expenses when it comes to commercial efforts and development efforts. So the economics for us is basically that we are getting a royalty in the low 20s in the U.S.

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes. All right. So since they will have the commercial sales force. But importantly, how does it work for dialysis? And how does it work for nondialysis? In dialysis, we all know that there's 2 big major players

Fresenius, DaVita, if I can believe Fresenius was at our conference. They didn't say anything yet because I don't think it's anything to say yet. But -- and then there's a smaller mom-and-pop type dialysis.

Do you need to get contracts at those centers? Are they studying your drug right now as we speak in a study? Would they be ready to go? And could you get contracts pretty quickly? How does that work in the dialysis?

Enrique A. Conterno

CEO & Director

Yes. Clearly, we have 2 very different segments in dialysis, nondialysis, not just the patients, but clearly who we are contracting with are different players, right?

As you mentioned, when it comes to dialysis, of course, it's the dialysis organizations. And this segment is highly concentrated. For us, I think one of the key catalysts for the broad use of roxadustat is going to be basically getting reimbursement. And that applies to both dialysis and nondialysis.

In the dialysis setting, that catalyst is driven by the event of having TDAPA eligibility, if the roxadustat is eligible for TDAPA and we're going to make efforts to try to submit as soon as we get approval to be able to ask CMS, make the submission and ask for that inclusion of roxadustat into TDAPA.

In terms of timing, the way we think about it is, we believe that it is possible, but it's also the earliest date that we could get TDAPA affective for roxa would be April 1 of 2021. I think that's a reasonable date, but it's also the earliest date because the effective date for TDAPA is typically at the start of each quarter.

And when it comes to the discussions with LDOs, clearly, we've worked with the large dialysis organization for quite some time. They were part of our Phase III trials. They are conducting Phase IIIb studies as we speak. Basically trying to -- clearly, the roxadustat's efficacy and safety is well documented now. But now they're starting it within their setting, which I think is going to be very helpful.

And now clearly, there are discussions, right, when it comes to thinking about the preparation for roxa to come into the market and which includes, of course, also contracting. AstraZeneca really takes the lead on those contracting discussions. FibroGen takes the lead on the discussion when it comes to the Phase IIIb studies. And clearly, we have excellent relationships with the large dialysis organization.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. So you have excellent relationships. They're testing the drug out in their own setting. Now there's trial programs going on. They're studying it to see how it impacts their flow. And they're aware of it. I think there's confusion or head scratching going on because people know that, for example, DaVita has a contract, supply contract, publicly with Amgen, and Fresenius is a large Mircera user. But you feel comfortable that there will be not 100% market share, but say, but there would be deals that can be in place so that you will see revenues there.

Enrique A. Conterno

CEO & Director

Yes. I base my confidence on the strength of that data, right? So if we think about roxadustat, there -if we just take -- look at the number of patients on dialysis, we have to start that there are a number of
those patients in dialysis. Most of them are treated for anemia, but we have about 15%, 20% of those
patients that are hyporesponsive, right? So where ESAs are really not working very well. Roxadustat
-- and they are in very high doses. roxadustat will be an excellent option there, okay? What about the
incident dialysis population, where we basically showed a very significant benefit when it comes to MACE
and MACE+.

So when we think about those, we believe that roxadustat, this is not a -- has -- is a very important option, I think, for the...

Michael Jonathan Yee

Jefferies LLC, Research Division

There's 2 populations there that logically makes sense. And the strength of the data alone, which is hyporesponders, which, by the way, we confirm with our own doctor checks that those guys are loss-making for the LDOs, by the way, right? You agree with that. They're loss-making.

Enrique A. Conterno

CEO & Director

Yes. That's right because there are very high doses. The payment is capitated.

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes, they're losing money on the bundle. And second of all, incident dialysis where there's strong cardiovascular data.

Enrique A. Conterno

CEO & Director

That's right. So this is just to say that we need to create a situation that is going to be a win-win for both the dialysis organization and of course, for the right patients to use roxadustat.

Michael Jonathan Yee

Jefferies LLC, Research Division

How confident are you that it will get it to TDAPA? I mean is that like that's straightforward like getting fast track or priority review? Or like, is there like a whole bunch of stuff that could happen and that's why, I don't think that's actually a huge breakthrough. Like what do we -- how do you explain that to somebody?

Enrique A. Conterno

CEO & Director

Yes, there's a very clear process how to apply for TDAPA, and we had the discussions with CMS. We think that we're going to be eligible. Of course, there's not a lot of presence for drugs that have gone through this process, which is different, maybe from a breakthrough designations or something like that. But we feel that the process is pretty clear. We think it's straightforward.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. I'm going to go read the documents online and figure this out. Okay. And how is it reimbursed? Like how does that workflow happen? So in the dialysis center, Sally comes in, she's at Fresenius, she used to get treated for the anemia, does the script and the prescription all get done there? Or does she get it at Walgreens? And how does all that work?

Enrique A. Conterno

CEO & Director

Clearly, when it comes to the dialysis organization, you basically have a highly integrated system, right, with important protocols and so forth. The -- one of the things that is important to understand, when we think about TDAPA, first of all, you basically have a system, there is a bundle. And keep in mind that the patient actually has a copay for that bundle of about 20%. TDAPA represents an additional payment, right, to the dialysis organization for the use, in this case, of roxadustat.

The patient will also have a copay on TDAPA of 20%.

Michael Jonathan Yee

Jefferies LLC, Research Division

So I know the bundle is about \$250 per treatment. If they want to get roxa, the dialysis company will purchase the bottle. And they will get reimbursed for that bottle using TDAPA.

Enrique A. Conterno

CEO & Director

That is correct. The reimbursement is basically 100% of the ASP price, at the average selling price. And when this is dispensed to the patient, the patient is responsible for 20% of that.

Michael Jonathan Yee

Jefferies LLC, Research Division

Makes sense. Okay, great. So that's helpful because, again, we're not -- nobody on Wall Street is particularly used to how that works. We're used to getting drugs either at the hospital into Medicare Part B or it's a Medicare Part D, which is at the pharmacy level. So -- okay, that's great.

Now how about nondialysis? How is that going to work? How does reimbursement work there? That's not to doubt, all right? Is that different situation. It's COVID, right? You have a nephrologist who's taking care of you. Maybe you just forget the script at the pharmacy. How is that different?

Enrique A. Conterno

CEO & Director

Yes, that is different because those patients basically will be getting their prescriptions, like you said, at the pharmacy, and you have very -- 3 different segments. I expect that in the case of roxadustat, about a little bit of north of 50%, it will be basically Medicare. So Part D, about 30% Commercial and then the rest Medicaid.

Michael Jonathan Yee

Jefferies LLC, Research Division

Medicaid, yes.

Enrique A. Conterno

CEO & Director

So those patients, yes, they will see their nephrologist. Keep in mind that those nephrologists also are basically part of treating patients with dialysis as well, right? So they have different types of patients, patients that are dialysis dependent and patients that are nondialysis dependent. So the experience on one setting, it's going to complement the other, right?

So it's -- and this particular case was going to be important, like I said, reimbursement is key. So we need to make sure that we are -- patients are going to have access. There are many ways that patients can have access, but longer term, clearly, formulary, having a formulary placement, I think, is key.

Clearly, Part D works differently from commercial and Medicaid, but I feel that we have a great partner that is going -- has been focusing on thinking about this and try to ensure that patients do have access and that we have the right formulary placement as soon as possible and the position as well for the patient.

Michael Jonathan Yee

Jefferies LLC, Research Division

Why -- I asked on this, the dynamic is different. Because it's not a bundled stuff, stuff like that. This is up straight for Medicare Part D. It should be no different than a cancer drug like Revlimid, you take at the pharmacy, you take it home. You pay your copay. And if it's commercial, you should be covered and there's a copay. That's just a formulary thing. You got to work to get the formulary contracts.

What I worry about is a COVID environment where patients may or may not be coming in as much if they're not on dialysis, right? How often do they see their doctors? Is there an urgency to get them on as quickly as in, or there's probably not going to be swapping, so it's more just -- maybe just talk a little

bit about that and if there is -- is there less reason to have a black box there or more? Maybe is this somewhat challenging than dialysis?

Enrique A. Conterno

CEO & Director

Yes. I think it's a good question for us to think about COVID. I think we have a few things that are working in our favor. So I'm going to call them important tailwinds, when it comes -- keep in mind that, number one, that AstraZeneca has a renal presence already, okay?

And that renal presence -- so they already have a sales force. They have presence, including the renal presence, with a presence in the dialysis organization.

So that is hugely important because keep in mind of those relationships exist with the customers, right? That's very different from trying to have a new sales force, establish new relationships during COVID time. So...

Michael Jonathan Yee

Jefferies LLC, Research Division

They're very good, and that's why you did that partnership. I have too many small biotechs that are struggling right now during cover. Yes. So yes, that is AstraZeneca that will be doing that. Okay. That's number one.

Enrique A. Conterno

CEO & Director

Correct. So now clearly, one of the things that we need to -- when it comes to patients in the NDD setting, we need to create an urgency for treating anemia because today, this is very much undertreated. I know people ask me, well, are we going to convert patients from ESAs and so forth. Keep in mind that the number of patients that are being treated is a very -- it's really in single digits, when it comes to the overall potential addressable market. So for us...

Michael Jonathan Yee

Jefferies LLC, Research Division

This is not \$1 billion, though. Just -- dollar-wise, it's about \$1 billion. I think it's about \$1 billion it checked my market model. But the number of patients is small relative to the size, but it is doing about \$1 billion.

Enrique A. Conterno

CEO & Director

Yes, it is still significant. But think about what the potential market is. And I -- you asked about how to create that urgency. Clearly, one of the things that we've shown with our data is a very significant decrease in transfusions -- blood transfusions.

This is extremely important for patients. You talk to a patient, and you ask, clearly, avoiding that is very important. And we didn't have just a small decrease. We basically -- when we look at time to transfusion, we basically -- the hazard ratio was 0.26 very, very significant benefit.

In addition, you asked me about this as well. But as you know, we basically, recently shared some data around roxadustat and how you basically see different levels of hemoglobin achievement and correlating that to making it.

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes.

Enrique A. Conterno

CEO & Director

And what we saw was basically that for low levels of hemoglobin, below 8 and even below 10, you basically see a much higher mass events and you really -- as you correct and maintain that, you start seeing a much lower level of events.

So that's another, I think, important aspect because I think the importance of the data is, it's important to treat anemia. You are basically trying to reduce blood transfusions and so forth, but it is pretty clear when the hemoglobin is way too low, people are going to be at much higher risk of mass events.

Michael Jonathan Yee

Jefferies LLC, Research Division

Do you think you'll see some swapping? Is that the lower hanging fruit? Or do you think it's new patients coming on to you -- didn't want EPO? Maybe talk about that. If you had it, yes, a year or 12 months from now.

Enrique A. Conterno

CEO & Director

I think in the NDD setting, you will see some swapping just because roxadustat is going to be -- all of the benefits, but it's also so much more convenient for patients.

Michael Jonathan Yee

Jefferies LLC, Research Division

Right, yes.

Enrique A. Conterno

CEO & Director

But honestly, I don't see that as the long-term reason where we should feel confident about what we could achieve. I think what we need to look at is not just are we converting those patients. But how we're raising the treatment rates because at the end, that's really the long-term opportunity that we see.

Keep in mind that when we think about those segments, DD and NDD, we always say that DD should be up to a faster uptick, a lot of control from protocol perspective, from dialysis organizations, that they can basically roll out.

But when it comes to NDD, while the uptick might be slower, so we expect more than 50% of our revenues initially to come from DD. Longer term, I view NDD as larger, including, I would say, much larger than DD, but we need to do the work to basically build that market.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. Well, this is why people are positive in the long term, but they also -- you know how Wall Street works, the first 3 or 4 quarters where people get a look at what you're telling me. Are you telling me it's big Enrique, why are the sales not big? So that's the test that people put you up in the first few quarters.

Enrique A. Conterno

CEO & Director

Well, we got a -- there's no future without the present. So you got to deliver in the near-term and in the long term.

Michael Jonathan Yee

Jefferies LLC, Research Division

One other question, too, that I think is important in nondialysis and dialysis is what you can get in the label. Can you get secondary endpoint things like incident dialysis, cardiovascular benefit? Can you get time to transfusion? I look at a lot of labels. I rarely see secondary endpoints in there.

Enrique A. Conterno

CEO & Director

Yes. So clearly, this is part of the discussion with the FDA, I think, from FibroGen's perspective, the more of our clinical data that we can include in the label, that's positive for us, right? So -- but I won't be able to comment beyond that until we basically have the label.

Michael Jonathan Yee

Jefferies LLC, Research Division

All right. I just -- I really see much secondary endpoints. That's also -- I'm hopeful, but I don't know. Okay.

So one last step because you did mention at the beginning of this. I think it's important, let's say, a 12 and 18-month view that MDS could be a pretty large opportunity. Now frame it for people because the Phase III is going on in MDS. I thought that the data is in '21, but I think it's '22, but correct me if I'm wrong.

And is it literally, do I need to track luspatercept sales from Acceleron like -- or is that actually under representing what you could do because they're only, I believe, in are as positive patients. So are you telling me your drug could basically be used in front of -- instead of luspatercept, they're doing \$800 million a year, annualized?

Enrique A. Conterno

CEO & Director

Yes. I -- so clearly, that speaks, I think, the need in this particular setting for these patients. We expect to have the readout in the first half of 2022, that's -- we think that's an important opportunity. Clearly, this is an important Phase III study, is the next indication for roxa. You're right, we are basically studying patients irrespective of sideroblast status.

So we will be basically looking at all of those low-risk MDS patients. When we think about luspa, they are basically doing well, but they do have -- they're going after a much smaller segment. That might be, maybe 30%, 40% of the overall opportunity that we will go after.

Now there's a pretty big difference between them and us, and that is, we're going to be bound by some of our pricing that we have in CKD, right? So the price level is going to be guite different.

Michael Jonathan Yee

Jefferies LLC, Research Division

Now, how different is that? That's important. Thank you for clarifying that.

Enrique A. Conterno

CEO & Director

Yes, it is pretty significant. I don't recall the exact price of luspa, but it might be in the 150,000 plus per year, right? So now we still believe this is an important opportunity, relative to CKD is much smaller. The opportunity that is more comparable to CKD is the opportunity in CIA, chemo-induced anemia, a very significant opportunity. We expect data, as I mentioned, in the second half of -- for our Phase II of next year, potentially spilling into the first half.

So we're excited about that data. We will assume that is positive, we will start a Phase III trial immediately.

But that opportunity, I think of it from a size perspective is almost as large as CKD.

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes. I need to think about that a bit because I think Amgen got in trouble because they were actually running survival studies. I mean, is it still -- is EPO used at all in CIA or no?

Enrique A. Conterno

CEO & Director

Very little. Clearly, so that the use in CIA for ESA is used to be very significant. At some point in time, it might have been a \$4 billion market. That use today is significantly below that.

Michael Jonathan Yee

Jefferies LLC, Research Division

Right. So just to be clear, because you use chemotherapy, which is still billions of dollars, everyone of those people get anemia, they were giving EPO to treat that. Not because of any kidney problems because of the chemo, and people were doing that. When they ran the survival studies and showed as a negative impact on survival in cancer, people thought, well, why would I be giving this drug to cancer patients to treat the chemotherapy-induced anemia, could be actually feeding more oxygen to the tumor. So isn't that a problem? Just to be clear.

Enrique A. Conterno

CEO & Director

Clearly, we need to run the studies. But as you know, our roxadustat has a very different mechanism than EPO. So we think it's a much more natural way for the body to basically respond, right?

So we are excited, we're conducting the Phase II. We'll look at the Phase II data, of course, and we'll decide based on the data. But it is pretty clear that investigators are extremely interested or at least this is the case.

Michael Jonathan Yee

Jefferies LLC, Research Division

Fantastic. Well, so I want to ask one last question, and we'll save pamrevlumab for a different discussion because, obviously, we have a lot of roxa stuff coming up. But we have a PDUFA date at the end of the year. So we're just waiting on an announcement for that. And then whenever you get something, you'll let us know?

Enrique A. Conterno

CEO & Director

Absolutely. We're very excited. As I mentioned, we are -- FibroGen has been working on roxadustat for quite some time. So this is an incredibly important milestone for the company. We just need to make sure that we do our part to be prepared for a very successful launch. So that as many patients can benefit.

Michael Jonathan Yee

Jefferies LLC, Research Division

Who handles the NDA, who is -- is that Astra that's handling, or that's you handling the NDA. Who actually is handling the paperwork?

Enrique A. Conterno

CEO & Director

It is FibroGen. So FibroGen is the sponsor of the NDA. Eventually, that will go to AstraZeneca post approval.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. All right. Well, I look forward to it. I'll be checking my e-mail every day between now and December 20, and wishing you good luck.

So thank you, Enrique, for being here with us. Good luck, and in the end of the year we'll be here with you, and thank you for being here with us.

Enrique A. Conterno

CEO & Director

Thank you very much, Michael. I appreciate the invitation.

Michael Jonathan Yee

Jefferies LLC, Research Division Thanks, Enrique.

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EXHIBIT JJ



Investors and Media

Press Release



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FibroGen Announces Retirement of K. Peony Yu, M.D., and Appointment of Mark Eisner, M.D., M.P.H. as Chief Medical Officer

SAN FRANCISCO, Dec. 01, 2020 (GLOBE NEWSWIRE) -- FibroGen, Inc. (NASDAQ: FGEN) today announced the retirement of K. Peony Yu, M.D., Chief Medical Officer, and appointment of Mark Eisner, M.D., M.P.H. in that role. Dr. Yu will continue as Chief Medical Officer through December 20, 2020, the roxadustat PDUFA date, and will remain with FibroGen through March 15, 2021 serving as Executive Advisor to the CEO to support the transition.

Dr. Yu joined FibroGen in 2008 and has provided key leadership for global clinical development across the company, leading the development of roxadustat in multiple indications and advancement of the overall portfolio.

"On behalf of the board, shareholders, and our employees, I want to thank Peony for her tremendous contributions as Chief Medical Officer of FibroGen," said Enrique Conterno, Chief Executive Officer, FibroGen. "With her considerable expertise and leadership, roxadustat was approved in China and Japan for the treatment of CKD anemia with pending regulatory decisions in the US, EU, and additional countries, to potentially serve millions of patients worldwide."

"It has been my privilege to work with many talented colleagues at FibroGen to make a difference in the lives of many," said Dr. Yu. "I look forward to our upcoming roxadustat U.S. PDUFA date, and expect FibroGen will continue to advance important new medicines."

Mark Eisner, M.D., M.P.H. has joined FibroGen as of today, and will become Chief Medical Officer effective December 21, 2020, overseeing all global clinical development and regulatory affairs for FibroGen. Dr. Eisner has nearly 30 years of academic, biopharmaceutical, and drug development experience, from early clinical phase through post-commercialization.

"Mark's extensive leadership, clinical development, and regulatory expertise come at a critical time for the company as we accelerate our development and look ahead to multiple significant clinical milestones. The depth and breadth of his therapeutic development experience is an ideal fit, and we are thrilled to welcome him to the FibroGen team," said Enrique Conterno, Chief Executive Officer, FibroGen. "We look forward to Mark's contributions as a proven business leader, clinician, and researcher in our continued evolution toward becoming a commercial-stage biopharmaceutical company with a maturing clinical pipeline."

"I am excited to lead the clinical development organization during this important time at FibroGen, when the company is rapidly advancing its robust late-stage pipeline," said Dr. Eisner. "I look forward to progressing the current clinical studies to bring valuable medicines to patients."

Dr. Eisner, who brings more than 10 years of experience in clinical drug development and 20 years as a practicing physician, has held leadership positions in academic medicine, clinical research, and pharmaceutical development. In 2010, he joined Genentech, a member of the Roche Group, and was most recently Senior Vice President and Global Head of Product Development Immunology, Infectious Disease, and Ophthalmology where he led clinical development for areas including respiratory medicine, rheumatology, nephrology, inflammatory bowel disease, virology, and retinal disease.

Prior to Genentech, Mark was Professor of Medicine and Anesthesia at the University of California San Francisco where he was an internationally recognized expert on clinical research in acute and chronic lung disease. He served as a steering committee member and ultimately UCSF Principal Investigator for the National Heart, Lung, and Blood Institute ARDS Clinical Trials Network which conducted several clinical landmark trials. Mark also built a world-class NIH-funded clinical research program focusing on the epidemiology and long-term health outcomes of obstructive lung disease.

He was also an investigator in the UCSF Cardiovascular Research Institute. Mark published ~200 peer-reviewed articles, served on multiple NIH study sections, and was a member of the American Thoracic Society Board of Directors.

Mark graduated from Stanford University with an A.B. degree in Human Biology and then received his M.D. degree from the University of Pennsylvania School of Medicine. He completed residency training in internal medicine, served as Chief Medical Resident, and pursued advanced fellowship training in pulmonary and critical care medicine at the University of California, San Francisco. He also received a M.P.H. degree from the University of California, Berkeley School of Public Health.

About FibroGen

FibroGen, Inc. is a biopharmaceutical company committed to discovering, developing and commercializing a pipeline of first-in-class therapeutics. The company applies its pioneering expertise in hypoxia-inducible factor (HIF) and connective tissue growth factor (CTGF) biology to advance innovative medicines for the treatment of unmet needs. The Company is currently developing and commercializing roxadustat, an oral small molecule inhibitor of HIF prolyl hydroxylase activity, for anemia associated with chronic kidney disease (CKD). Roxadustat is also in clinical development for anemia associated with myelodysplastic syndromes (MDS) and for chemotherapy-induced anemia (CIA). Pamrevlumab, an anti-CTGF human monoclonal antibody, is in clinical development for the treatment of idiopathic pulmonary fibrosis (IPF), locally advanced unresectable pancreatic cancer (LAPC), Duchenne muscular dystrophy (DMD), and coronavirus (COVID-19). For more information, please visit www.fibrogen.com.

Forward-Looking Statements

This release contains forward-looking statements regarding our strategy, future plans and prospects, including statements regarding the development and commercialization of the company's product candidates, our clinical programs and regulatory events and those of our partners, and the commercial prospects of roxadustat. These forward-looking statements include, but are not limited to, statements about our plans, objectives, representations and contentions and are not historical facts and typically are identified by use of terms such as "may," "will", "should," "on track," "could," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential," "continue" and similar words, although some forward-looking statements are expressed differently. Our actual results may differ materially from those indicated in these forward-looking statements due to risks and uncertainties related to the continued progress and timing of our various programs, including the enrollment and results from ongoing and potential future clinical trials, and other matters that are described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and our Quarterly Report on Form 10-Q for quarter ended September 30, 2020 filed with the Securities and Exchange Commission (SEC), including the risk factors set forth therein. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and we undertake no obligation to update any forward-looking statement in this press release, except as required by law.

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Source: FibroGen, Inc

EXHIBIT KK



9 December 2020

Division of Dockets Management U.S. Food and Drug Administration (HFA-305) Room 1061 5630 Fishers Lane Rockville, MD 20852

> Re: Citizen Petition by Epstein Becker & Green Regarding the Pending New Drug **Application for Roxadustat [Docket: FDA-2020-P-2193]**

Dear Sir or Madam:

On behalf of FibroGen, Inc., I write to strongly object to the November 13, 2020 Citizen Petition titled, "Citizen Petition for FDA to Require Adequate Cardiovascular Safety and All-Cause Mortality Data Be Submitted to FDA for Review Before Approving Roxadustat (FG-4592) for the Treatment of Anemia in Patients with Chronic Kidney Disease (CKD), and Require a Boxed Warning." As detailed in these comments, the above-referenced Citizen Petition is without scientific or legal basis, and bears all of the hallmarks of citizen petitions that are submitted with the intent of delaying competition.

This Citizen Petition was submitted by the law firm Epstein Becker & Green on behalf of an unnamed client. Although the Petition purports to raise concerns based on "recently published data," the cited clinical trial data was presented over one year ago and was disseminated publicly, including at American Society of Nephrology Kidney Week 2019. Soon thereafter, on December 20, 2019, FibroGen submitted to FDA the New Drug Application (NDA) for roxadustat for the treatment of anemia of chronic kidney disease, in both non-dialysis-dependent and dialysis-dependent CKD patients. Now, many months later, and just weeks before the December 20, 2020 Prescription Drug User Fee Act (PDUFA) date for the FibroGen application, Epstein Becker & Green, on behalf of an unnamed client, presumably with a commercial interest, emerges with a spurious critique of the roxadustat data.²

In fact, the purported concerns presented in the Citizen Petition are unfounded and misconstrue the

¹ See Citizen Petition at 7.

² To the extent the Citizen Petition is in fact motivated by competitive concerns, FDA has extensively addressed the anticompetitive impact of citizen petitions in the context of abbreviated and 505(b)(2) new drug applications, and many of the same concerns would apply in this case. Simply put, Epstein Becker & Green's spurious arguments place an unnecessary, last minute burden on FDA by forcing the agency to respond, in a limited period of time, to an incorrect and misleading characterization of data that has long been available to the petitioner. As former FDA Commissioner Scott Gottlieb stated in the generic drug context, citizen petitions submitted to block competitors are an "abuse of this system" and "add to resource burdens on the generic drug review process and the FDA's regulatory decision making." Statement from FDA Commissioner Scott Gottlieb, M.D., on New Agency Actions to Further Deter 'Gaming' of the Generic Drug Approval Process by the Use of Citizen Petitions (Oct. 2, 2018), https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scottgottlieb-md-new-agency-actions-further-deter-gaming-generic-drug.



results from a global Phase 3 program encompassing 15 trials that enrolled more than 10,000 patients, worldwide, and which for the US NDA submission included primary analyses from over 8,000 patients. The petitioner is not aware of all of the data and analyses that have been presented to the FDA, and makes erroneous assumptions and claims based on their incomplete understanding of the data.

The Phase 3 program demonstrated that roxadustat is effective in both dialysis dependent chronic kidney disease (DD-CKD) and non-dialysis dependent chronic kidney disease (NDD-CKD) patients. Importantly, the pre-specified primary efficacy endpoint of hemoglobin change from baseline at Weeks 28 to 52 was met in each of the NDD-CKD Phase 3 studies and each of the DD-CKD Phase 3 studies.

Cardiovascular safety of roxadustat was also carefully evaluated, and demonstrated in the Phase 3 program, by assessment of major adverse cardiovascular events (MACE) from pooled analyses of Phase 3 studies. In the MACE analysis of the DD-CKD patient pool, roxadustat demonstrated non-inferiority compared to epoetin-alfa, and in the NDD-CKD pool, roxadustat demonstrated non-inferiority to placebo with respect to MACE.

Moreover, despite the petitioner's erroneous claims, placebo is an appropriate comparator for a study in NDD-CKD, as in the 12 months prior to dialysis initiation less than 15% of CKD patients receive treatment with erythropoietin stimulating agents (ESA), while the average hemoglobin level at dialysis initiation is as low as 9.3 g/dL (USRDS Annual Data Report 2020). With respect to the use of iron supplementation in this population, iron therapy was permitted a concomitant treatment in FibroGen's Phase 3 NDD-CKD studies.

In addition to cardiovascular safety, reduction of transfusion is a fundamental aim of anemia treatment, as transfusion carries with it significant safety risks for the patient. Importantly, in each of the Phase 3 NDD-CKD clinical studies, the proportion of patients requiring red blood cell transfusion was lower in patients treated with roxadustat.

FibroGen's NDA submission was complete, complied with all FDA guidance, and included data from all clinical and preclinical studies. The Integrated Summary of Safety cardiovascular safety report includes the pooled cardiovascular safety analyses of the DD-CKD, and NDD-CKD patient populations. In addition, for completeness and full transparency, FibroGen included certain cardiovascular safety sensitivity analyses, including the stable dialysis subgroup, and the DD-CKD pool including the PYRENEES study. The results from these sensitivity analyses do not change the conclusions with respect to MACE of non-inferiority of roxadustat to epoetin-alfa in DD-CKD patients, and non-inferiority of roxadustat to placebo in NDD-CKD patients.

In conclusion, FibroGen's NDA submission was complete and transparent. The data supporting the safety and effectiveness of roxadustat is robust and compelling. The petitioner is not aware of the contents of FibroGen's submission, and has made several incorrect assumptions and spurious arguments. FibroGen remains committed to developing innovative medicines to address unmet medical needs for patients. Based on the foregoing, we ask FDA to deny the above-referenced Citizen Petition.



Thank you for attention to this important matter. We look forward to continuing to work with FDA during the NDA review of roxadustat.

Respectfully submitted,

R Wayne Frost Digitally signed by R Wayne Frost DN: cn=R Wayne Frost, o=FibroGen, ou=Regulatory Affairs, email=wfrost@fibrogen.com, c=US Date: 2020.12.09 17:22:16 -08'00'

R. Wayne Frost, Pharm.D., J.D. Senior Vice President Regulatory Affairs and Medical Writing

EXHIBIT LL



Investors and Media

Press Release



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FibroGen Provides Regulatory Update on Roxadustat

SAN FRANCISCO, March 01, 2021 (GLOBE NEWSWIRE) -- FibroGen, Inc. (Nasdaq: FGEN) and its partner, AstraZeneca (LSE/STO/Nasdaq: AZN), today announced that the Cardiovascular and Renal Drugs Advisory Committee of the U.S. Food and Drug Administration (FDA) will hold an advisory committee (AdCom) meeting to review the new drug application for roxadustat in the U.S. The companies have not received a confirmed AdCom meeting date from the FDA.

"While disappointed with the news today, FibroGen and AstraZeneca are committed to working with the FDA to bring roxadustat to patients with anemia of CKD in the U.S. as soon as possible," said Enrique Conterno, Chief Executive Officer, FibroGen. "We continue to be confident in the efficacy

and safety profile of this potential new medicine based on positive results from a global Phase 3 program encompassing more than 8,000 patients."

Roxadustat has been approved in China, Japan and Chile for the treatment of anemia of CKD in both non-dialysis dependent (NDD) and dialysis-dependent (DD) adult patients.

Roxadustat, an oral small molecule hypoxia-inducible factor prolyl hydroxylase (HIF-PH) inhibitor, is the first HIF-PH inhibitor accepted by the FDA for review for the treatment of anemia of CKD.

About Anemia of CKD

Chronic kidney disease (CKD) is generally a progressive disease characterized by gradual loss of kidney function that may eventually lead to kidney failure or end stage renal disease, requiring dialysis or kidney transplant. CKD is estimated to occur in approximately 10-12% of adults worldwide and is predicted to become the fifth most common cause of premature death globally by 2040.

Anemia, a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, is a common early complication of CKD, affecting approximately 20% of CKD patients. Anemia of CKD is associated with an increased risk of hospitalization, cardiovascular complications, and death, and can also cause significant fatigue, cognitive dysfunction and reduced quality of life. Blood transfusions are used for treating severe anemia, however, they may reduce a patient's opportunity for kidney transplant and can increase the risk of infection and/or complications such as heart failure and allergic reactions.

About Roxadustat

Roxadustat, an oral medicine, is the first in a new class of medicines, HIF-PH inhibitors that promote erythropoiesis, or red blood cell production, through increased endogenous production of erythropoietin; improved iron absorption and mobilization; and downregulation of hepcidin. Roxadustat is also in clinical development for anemia associated with myelodysplastic syndromes (MDS) and for chemotherapy-induced anemia (CIA).

Roxadustat is approved in China, Japan, and Chile for the treatment of anemia of CKD in adult patients on dialysis (DD) and not on dialysis (NDD). In Europe, the Marketing Authorization Application for roxadustat for the treatment of anemia of CKD in patients both on dialysis and not on dialysis was filed by our partner Astellas and accepted by the European Medicines Agency for review on May 2020. Several other licensing applications for roxadustat have been submitted by Astellas and AstraZeneca to regulatory authorities across the globe, and are currently in review.

Astellas and FibroGen are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia in territories including Japan, Europe, Turkey, Russia and the Commonwealth of Independent States, the Middle East, and South Africa. FibroGen and AstraZeneca are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia in the U.S., China, other markets in the Americas, in Australia/New Zealand, and Southeast Asia.

About FibroGen

FibroGen, Inc. is a biopharmaceutical company committed to discovering, developing, and commercializing a pipeline of first-in-class therapeutics. The Company applies its pioneering expertise in hypoxia-inducible factor (HIF) and connective tissue growth factor (CTGF) biology to advance innovative medicines for the treatment of unmet needs. The Company is currently developing and commercializing roxadustat, an oral small molecule inhibitor of HIF prolyl hydroxylase activity, for anemia associated with chronic kidney disease (CKD). Roxadustat is also in clinical development for anemia associated with myelodysplastic syndromes (MDS) and for chemotherapy-induced anemia (CIA). Pamrevlumab, an anti-CTGF human monoclonal antibody, is in clinical development for the treatment of locally advanced unresectable pancreatic cancer (LAPC), Duchenne muscular dystrophy (DMD), and idiopathic pulmonary fibrosis (IPF). For more information, please visit www.fibrogen.com.

Forward-Looking Statements

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Source: FibroGen, Inc

EXHIBIT MM

S&P Global Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN FQ4 2020 Earnings Call Transcripts

Monday, March 01, 2021 10:00 PM GMT

S&P Global Market Intelligence Estimates

	-FQ4 2020-		-FQ1 2021-	-FY 2020-			-FY 2021-	
	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS	CONSENSUS	ACTUAL	SURPRISE	CONSENSUS
EPS Normalized	(0.19)	(0.64)	NM	(0.23)	(1.65)	(2.11)	NM	(0.99)
Revenue (mm)	100.82	65.00	V (35.53 %)	111.70	212.09	176.32	V (16.87 %)	479.74

Currency: USD

Consensus as of Feb-19-2021 1:12 PM GMT



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Call Participants

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Presentation

Operator

Ladies and gentlemen, thank you for standing by, and welcome to the FibroGen Fourth Quarter and Full Year 2020 Financial Results Conference Call. [Operator Instructions]. Please be advised for today's conference is being recorded. [Operator Instructions].

I would now like to hand the conference over to your speaker today, Mr. Michael Tung. Thank you, please go ahead.

Michael Tung

Investor Relations Executive

Thank you, Lindon, and good afternoon, everyone. I'm Michael Tung, Vice President of Corporate Strategy and Investor Relations at FibroGen. Joining me on today's call are Enrique Conterno, our Chief Executive Officer; Dr. Percy Carter, our Chief Scientific Officer; Pat Cotroneo, our Chief Financial Officer; Mark Eisner, our Chief Medical Officer; Thane Wettig, our Chief Commercial Officer; Chris Chung, our Senior Vice President of China operations; and Dr. Elias Kouchakji, our Senior Vice President of Clinical Development, Drug Safety and Pharmacovigilance.

The format for today's call includes prepared remarks from Enrique and Pat, after which we will open up the call for Q&A. I would like to remind you that remarks made on today's call include forward-looking statements about FibroGen. Such statements may include, but are not limited to, our collaborations with AstraZeneca and Astellas, financial guidance, the initiation, enrollment, design, conduct and results of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities, commercial results and results of operations, and risks related to our business, and certain other business matters.

Each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those projected in that statement. A more complete description of these and other material risks can be found in FibroGen's filings with the SEC, including our most recent Form 10-K and Form 10-Q. FibroGen does not undertake any obligation to update publicly any forward-looking statements. Whether as a result of new information, future events or otherwise.

The press release reporting our financial results and business update and a webcast of today's conference call can be found on the Investors section of FibroGen's website at www.fibrogen.com. With that, I would like to turn the call over to Enrique Conterno, our CEO. Enrique?

Enrique A. Conterno

CEO & Director

Very good. Thank you, Mike, and good afternoon, everyone, and welcome to our fourth quarter and full year 2020 earnings call. I intend to reflect on my first year as CEO of FibroGen by providing a high-level summary of important accomplishments and developments, not only in recent months, but also for 2020. Pat Cotroneo, our CFO, will then review the financials, after which, we will open the call for your questions.

I continue to be confident in my assessment of FibroGen has a unique opportunity to create significant value for patients and shareholders by executing on our 3 areas of focus: number one, ensuring regulatory and commercial success of roxadustat, a transformational medicine for the treatment of anemia, first in patients with chronic kidney disease and with significant potential for expansion to additional indications. Number two, accelerating the development of pamrevlumab in 3 high value indications, locally advanced unresectable pancreatic cancer, Duchenne muscular dystrophy and idiopathic pulmonary fibrosis. And number three, strengthening our research capabilities to maximize our scientific and medical leadership position in both HIF and CTGF biology. In addition, we are focused on expanding our clinical development pipeline by evaluating both internal and external opportunities to address unmet medical needs.

Today's call will include a review of roxadustat, our continued strong performance in China and our clinical trial programs. Let us get started with the roxadustat new drug application or NDA review. Last December, in the final stages of review, the FDA extended the review period of the NDA by 3 months to review additional analysis of existing clinical data and set a new PDUFA date of March 20, 2020 first. Just today, we were informed by the FDA that they plan to hold as an advisory committee, or Adcom meeting to review the NDA for roxadustat in the U.S. We have not received a schedule for the planned Adcom. We are surprised by the timing of this request. On 3 separate occasions, the FDA indicated they were not planning to hold an Adcom at the time. First, when the NDA filing was accepted, then after the mid-cycle review. And finally, after the late cycle review. It would not be unusual for the FDA to hold an Adcom for a first-inclass new molecular entity. And as communicated last spring, we were preparing for this possibility.

We will now resume those preparation activities and look forward to presenting the comprehensive roxadustat data. We continue to have confidence in the completeness of our NDA submission and the strength of our data and FibroGen and AstraZeneca are committed to working with the FDA to bring roxadustat to patients with anemia CKD in the U.S.

As you can appreciate, it has been the case throughout the final stages of review, we will not be able to discuss the details of our FDA interactions. Our pre-commercial activities continued as planned. FibroGen had its largest presence ever at the American Society of Nephrology Kidney Week conference in October of last year, and there continues to be significant interest in roxadustat from the clinical community. The momentum generated at ASN continues with additional analysis and planned disclosures of our Phase III data in order to maintain our HIF-PHI scientific and clinical leadership position.

Patient and healthcare professional disease education activities are ongoing and expecting to increase through the official launch. Our partner AstraZeneca has a comprehensive renal commercial presence in the U.S. and together, we're committed to make roxadustat available to as many CKD patients as quickly as possible. To optimize patient access, AstraZeneca is leading the discussions with both the houses organizations and payers who cover non-dialysis patients. We have submitted manuscripts covering the Phase III studies for CKD anemia to peer-reviewed journals. As you can see on the slide 5 of these manuscripts have been published, covering nondialysis-dependent, dialysis-dependent and incident dialysis data. Details on these publications can be found in our press release, and we expect additional publications of Phase III data in the coming months.

In Japan, our partner, Astellas, received an additional advance approval for the treatment of anemia CKD in adult patients not on dialysis in November of 2020. In addition, in December of 2020, the 14-day prescription rule was lifted for Evrenzo. As a result of these 2 events, Astellas has seen an acceleration in a Evrenzo's uptake. The European Medicines Agency accepted the roxadustat marketing authorization application for the treatment of anemia in adult patients with chronic kidney disease, both on dialysis and not on dialysis in May of 2020. We expect a decision midyear.

Now -- moving now to China. We're pleased to report net sales of roxadustat of \$29.2 million for the fourth quarter versus \$22.7 million in the third quarter. The total net roxadustat sales in China for 2020, the first year, roxadustat was included in the NRDL, were \$72.5 million. The continuing increase in uptake is being driven by both an expansion in hospital listings and broad adoption within listed hospitals. Hospital listings continue to be a key focus of our launch efforts. Notably, as of the end of the year, roxadustat was listed at hospitals, representing approximately 70% of the CKD anemia market opportunity in China. This is in comparison to 55% at the end of the third quarter. We're driving towards our goal of making roxadustat, the #1 treatment option for anemia CKD patients in China.

We continue to see significant roxadustat utilization across a range of anemia of CKD patient populations. Approximately 60% of patients treated with roxadustat in China are on dialysis, split between hemodialysis and peritoneal dialysis. Within hemodialysis, initial adoption has been in patients who do not respond well to ESAs as well as in incident dialysis patients. The remaining 40% of roxadustat-treated patients are CKD anemia patients not on dialysis. This broad utilization pattern bodes well for long-term success and provides critical earnings as we prepare to launch roxadustat in the U.S. and in other countries. We look forward to keeping you updated as we advance our long-term goal of making roxadustat the standard of care in treating China's CKD anemia patients.

Moving now to our clinical development. On our third quarter earnings call, we provided timeline guidance for most of our clinical trials. We are reiterating that guidance today. And do not intend to update this guidance on a quarterly basis, but it's not only where we have meaningful changes. Starting with roxadustat. We recently completed enrollment in WHITNEY, our Phase II trial in patients with chemotherapy-induced anemia and top line data is expected in the second half of this year. On conclusion of this trial, if successful, we plan to initiate a Phase III program in collaboration with AstraZeneca and Astellas. MATTERHORN, our Phase III travel in patients with anemia of myelodysplastic syndrome or MDS, continues to enroll with top line data expected in the first half of 2022. Finally, we recently completed enrollment of ASPEN and DENALI, two Phase IIIB studies of roxadustat in CKD anemia with large dialysis organizations in the United States.

Moving now to pamrevlumab. In locally advanced unresectable pancreatic cancer, our LAPIS Phase III trial is enrolling well, with top line resection data expected in the second half of 2022. Moving to the Duchenne muscular dystrophy, enrollment continues in our LELANTOS Phase III trial in nonambulatory patients with top line data also expected in the second half of 2022. Finally, in idiopathic pulmonary fibrosis, we recently initiated our ZEPHYRUS-2 Phase III trial in December. IPF patients have severely compromised lung function and the current COVID situation continues to be extremely challenging for enrollment in both our private trials ZEPHYRUS and ZEPHYRUS-2. Despite these circumstances, we have activated a significant number of additional clinical trial sites and expanded geographically, including in China, such that when COVID improves, we should be in a position to accelerate enrollment in both trials expeditiously.

Given the different COVID scenarios, there is variability in our projected IPF timelines and we'll provide you with an update at the appropriate time. Accelerated enrollment of all of our ongoing clinical trials while ensuring patient safety continues to be a top priority.

Now let me touch briefly on the application of our pioneering expertise in hypoxia-inducible factor or HIF, 2-oxoglutarate [indiscernible] and connected tissue growth factor or CTGF biology, in order to advance innovative medicines for the treatment of anemia, fibrotic disease and cancer. In 2020, we completed a thorough internal review of all of our programs, and we plan to continue advancing internal molecules in our development pipeline. In addition, we are seeking to access external innovation.

Finally, it is my pleasure to address another important accomplishment, the hiring of significant leadership talent, which include the appointments of Dr. Percy Carter, as Chief Scientific Officer, Dr. Mark Eisner, as Chief Medical Officer; and Thane Wettig, as Chief Commercial Officer. In summary, 2020 was a productive transitional year and look forward to more progress against our stated goals in 2021.

I will now turn the call over to our CFO, Pat Cotroneo, for the financial update. Pat?

Pat Cotroneo

Chief Financial Officer

Thank you, Enrique. As announced today, total revenue for the fourth quarter of 2020 was \$65 million as compared to \$8 million for the fourth quarter of 2019. The current quarter revenue consists of net product revenues of \$29.2 million for roxadustat sales in China, \$21.5 million in development revenue and \$14.3 million in license revenue related to NDD approval in Japan. For the same period, operating costs and expenses were \$123 million and net loss was \$58.6 million or \$0.64 per basic and diluted share as compared to operating costs and expenses of \$108.4 million and a net loss of \$98.1 million or \$1.12 per basic and diluted share for the fourth quarter last year.

Included in operating costs and expenses for the quarter ended December 31, 2020, was an aggregate noncash portion totaling \$26.9 million, of which \$20.3 million was a result of stock-based compensation expense as compared to an aggregate noncash portion of \$22.1 million of which \$17.4 million was a result of stock-based compensation expense for the same period in the prior year.

At December 31, FibroGen had \$732.1 million in cash, cash equivalents, restricted time deposits, investments and receivables. At this time, I would like to outline some changes in financial reporting starting next quarter that result from the amendment to our China agreement with AstraZeneca. As we have previously reported, the amendment is expected to result in earlier and more consistent profitability

to FibroGen based on a continued 50-50 profit share with AstraZeneca. Under the amendment, we have formed a jointly owned distribution entity, the JDE, that began operations in Q1 2021. The JDE will be responsible for selling roxadustat to distributors and will pay for AstraZeneca's commercialization efforts in China and AZ's portion of profit share.

Previously, FibroGen was responsible for these items. The JDE is expected to account for over 95% of overall China roxadustat sales volume going forward. While the rest will continue to be conducted directly by FibroGen.

Starting in Q1 2021, FibroGen's revenue will be based on sales to the JDE at a transfer price as well as FibroGen's direct sales. The transfer price is expected to be in the range of 30% to 45% of JDE net sales, which reflects the JDE paying both AstraZeneca's commercialization expenses and AstraZeneca's portion of the profit share. In addition, to continue to provide context for the operating results of our roxadustat business in China, we also plan to share the overall net sales of roxadustat, i.e. the combination of end sales by AstraZeneca and end sales by FibroGen. Looking ahead, at our broader financial picture, we have a total of \$245 million of potential milestones expected this year for anticipated U.S. and EU approvals and first commercial sale in the U.S.

At this point in time, we have no changes in expectations in any of the anticipated milestones between now and the end of the year. Based on our latest forecast data, we estimate our 2021 ending balance of cash, cash equivalents, restricted time deposits, investments and receivables to be in the range of \$660 million to \$670 million, assuming U.S. and EU approval in 2021.

Thank you. And I would now like to turn the call back over to Enrique.

Enrique A. Conterno

CEO & Director

In closing, this is an important time for FibroGen. Roxadustat has launched in China, Japan and is under regulatory review in the U.S., Europe and other geographies. Pamrevlumab a wholly owned potential first-in-class new medicine. In Phase III developing the 3 value indications of locally advanced unresectable pancreatic cancer, Duchenne muscular dystrophy and idiopathic pulmonary fibrosis. We are re-energizing our research agenda to deliver on our unique scientific expertise. In parallel, we're building world-class research capabilities internally while also looking externally for opportunities. With the goal of expanding our pipeline of innovative drug candidates.

We have strengthened our leadership team, which will be instrumental for our strategic growth. We are in a strong financial position as roxadustat sales ramp up with approximately \$732 million in cash and another \$245 million in anticipated roxadustat milestone payments expected during 2021. Looking forward, I believe we're clearly positioned for success.

Now I would like to turn the call back to the operator for questions.

Question and Answer

Operator

[Operator Instructions]

Your first question comes from Joe Beatty from Citi.

Joel Lawrence Beatty

Citigroup Inc., Research Division

The first one is, are you able to share anything about the topics that you're preparing to address at the Adcom?

Enrique A. Conterno

CEO & Director

Thank you, Joel. Let me provide just a brief answer. I'm going to ask also Mark Eisner to comment. But clearly, at this point in time, we're not in a position to provide an update on that. As you know, there's typically a report that the FDA will basically make public prior to the Adcom. That's only a few days before the Adcom is actually held. We don't have a set date for the Adcom at this stage. And we do not provide to comment on our regulatory interactions with the FDA. Mark, I'm going to ask Mark Eisner, if he has any additional comments.

Mark Eisner

Chief Medical Officer

Yes. No, and thanks for the question. As you know, the FDA uses advisory committees to bring in external scientific, clinical or other perspectives into its review. And it would not be unusual to have an Adcom for first-in-class new molecular entity, in this case, what's surprising is the timing, as Enrique had alluded to in his introductory comments. At this point, we're going to resume our preparation activities for the advisory committee and we look forward to presenting the comprehensive roxadustat program and its data. We continue to have confidence in the completeness of our NDA submission, the strength of our data and along with our partner, AstraZeneca, we're committed to working together with the FDA to bring roxadustat to patients with anemia of CKD in the U.S. So thanks again for the question.

Joel Lawrence Beatty

Citigroup Inc., Research Division

And then maybe one follow-up to that. Can you share anything about how you and AstraZeneca collaborate for the Adcom preparations? And if there's one company taking the lead?

Enrique A. Conterno

CEO & Director

Yes. This is really a -- it has been a joint effort and joint process. Clearly, AstraZeneca has considerable expertise when it comes to Adcoms and we need to make sure that, that is being fully leveraged. But I think the -- when we were preparing back in the spring, that was the case, very collaborative. I expect that it will continue to be very much a joint effort.

Operator

Our next question comes from Michael Yee from Jefferies.

Michael Jonathan Yee

Jefferies LLC, Research Division

Two questions for you guys. You can understand that people are, I guess, confused and a bit perplexed by the timing and also just the chronology of how things are played out. So the first question is just, maybe, Enrique, can you just give us some comfort such that the discussions here or the debates or the issues

here are more of a labeling and black-box safety scenario question, such that whatever happens here, you don't believe that peak sales are likely to change too much? You've kind of made that comment before, but maybe you could comfort us in some way.

The second question is more of a logistical question for the team. I think that you can't really have 2 formal PDUFA extensions if you go look at documents. So do you just expect that we're going to pass the PDUFA date, how to deal with an Adcom? And then we just kind of go from there? Or do you expect that PDUFAs would actually be formally changed? So we would have some visibility on things?

Enrique A. Conterno

CEO & Director

Yes. Thank you for your question, Michael. Clearly, I think -- let me try to address maybe the first part -- the last part of your question. Our understanding is that the PDUFA date can be extended once that extension happens. So at this point in time, we expect that the PDUFA date will be missed. And therefore, we will have the Adcom at some point in time, but with no longer basically an active PDUFA date.

I think your next your -- the first part of your question was related to being more specific on the nature of the Adcom, clearly, when it comes to Adcoms, Adcoms are looking at the overall benefit risk profile of the product, of course, they try to get external scientific expertise to bear but I'm not in a position to be able to comment on the nature of that. And I think we have to prepare for it and I -- we want to see, of course, when this Adcom will be scheduled, we don't have a set date for it at this time. Keep in mind that we were notified of this today.

Operator

Your next question comes from Edwin Zhang from H.C. Wainwright.

Xiaodong Zhang

H.C. Wainwright & Co, LLC, Research Division

First one, how much do you think is this Adcom decision related to the new analysis you submitted to the FDA 2 months ago? And the second, just a follow-up on the PDUFA date. Just to clarify, are you going to get a new PDUFA date from the FDA or not? And when are we going to know the new PDUFA date, if there's one?

Enrique A. Conterno

CEO & Director

Yes. Yes. We don't believe there would be a new PDUFA date, given that there was already an extension. And I'm sorry, I missed the first part of your question.

Xiaodong Zhang

H.C. Wainwright & Co, LLC, Research Division

So how much do you see this Adcom decision from the FDA is related to the new analysis you submitted to the FDA 2 months ago?

Enrique A. Conterno

CEO & Director

Yes. We don't want to speculate.

Xiaodong Zhang

H.C. Wainwright & Co, LLC, Research Division

Okay. May be one more. Does this regulatory decision change your expectation of a clean or differentiated label compared to ESAs?

Enrique A. Conterno

CEO & Director

Yes. Listen, I think at this point in time, we have to go through the Adcom. We have a product with significant amount of clinical data. Keep in mind that our pivotal data for the U.S. included over 8,000 patients, we discussed that clinical data at length, we continue to stand behind our data and the strength of the data. Some of the data now has been published. There are 5 primary manuscripts that have been published, and a number of more that are upcoming. But at this point in time, I don't want to speculate on the nature of the Adcom. We very much look forward to have the opportunity to share the roxadustat data in a public forum.

Operator

Our next question comes from Geoffrey Porges from SVB Leerink.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

A number of questions related to this topic. First, Enrique, you're answering a lot of these regulatory questions. It would be helpful if the official regulatory representative for FibroGen could answer the questions. But why doesn't this amount to a complete response letter to your application? And particularly given the amount of time it's going to require to prepare a full company package and the FDA's package. It would seem certain that it's going to be much more than 30 days after the prior PDUFA date.

Secondly, it's going to certainly be hard for us and investors to be confident in your approval since -- as far as we know, you've replaced most people in the organization who are familiar with the very extensive amount of clinical data. And then lastly, could you confirm whether this review or whatever the Adcom is going to be, will it be held by the hematology division or the cardiorenal division, and will it be examining and hearing the objections from the citizens petitions?

Enrique A. Conterno

CEO & Director

Yes. So let me try to address some of your questions, but I am going to also ask Mark Eisner to maybe make some comments that he has formal -- as a Chief Medical also has regulatory responsibilities. First, this -- the advisory committee, we believe, is going to be the cardiorenal advisory committee. So that's how we understand it based on the communication with the FDA, which happened today. We -- I think you are making reference to Peony Yu's retirement as Chief Medical Officer. Keep in mind that Peony is still an employee of FibroGen at this stage. And she also has an agreement -- a consulting agreement over the next 6 months post her employment at here, at FibroGen to continue to provide advice. I feel that the strength of our team is considerable when it comes to roxadustat data, not just here at FibroGen but also AstraZeneca. And then I'm going to ask Mark Eisner to also provide some additional comments or add to what I'm sharing.

Mark Eisner

Chief Medical Officer

Yes. Thanks, Enrique. So the FDA did not issue a complete response letter. A complete response letter would indicate that the FDA had completed its review, the FDA review of our NDA is continuing and ongoing. And the FDA wants to have an advisory committee in order to bring external expertise, clinical, scientific and otherwise, into their review so that they can complete their review.

So it's a very different scenario to get an advisory committee compared to a complete response letter. I mean, to address the specifics of your timing, yes, it's a little late in the game under -- in the review process to get a request for an advisory committee, but the FDA is well within its rights and regulations to request an advisory committee at any time. And we're very willing and able to have this discussion in public and present our data, which, as we alluded to before, we're quite confident in.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

Mark, sorry, was this a change in the reviewing division, though, from the heme to the cardiorenal?

Mark Eisner

Chief Medical Officer

There was no change in the reviewing division. No.

Operator

Your next question comes from Annabel Samimy from Stifel.

Annabel Eva Samimy

Stifel, Nicolaus & Company, Incorporated, Research Division

I promise I won't ask about the Adcom because it doesn't seem like you can answer many of them, but maybe we can talk about some of the signals that you're getting ex U.S. Obviously, sales and churn are going well. The mix of sales dialysis to nondialysis is improving. Japan was approved in nondialysis, even the French issued temporary use authorization with treatment up to 12 grams per deciliter. So how should we read these signals abroad? And how can that help you and frankly, help you with the FDA to move this process along, can you draw from all of that information that is being generated globally? And given some of the movement that we're seeing in China, are you still assuming a \$500 million opportunity in China? Or is that a moving target?

Enrique A. Conterno

CEO & Director

Yes. No, I think what we said is that -- and we're very excited by the way, with the way our China business continues to progress. We have stated that we view the opportunity in China to be able to reach for roxadustat to be able to reach peak sales north of \$0.5 billion. It is pretty clear that the launch continues to go very well, and we expect continued growth in China as we look at 2021. So we're very excited about that.

We are -- indeed, we, of course, conduct pharmacovigilance activities in both China and Japan, where the product is launched. And we -- as you mentioned, we need to make this also matter when it comes to the average that we basically have and how the acceptance and adoption and the utility that the patient basically has in the countries where we're launching. So I think this is an important factor, of course.

Operator

Your next question comes from Jason Gerberry from Bank of America.

Jason Matthew Gerberry

BofA Securities, Research Division

Just from a timing perspective, just so as we think about potentially modeling the timing implications here. So it sounds like it's a moving target with at least a 55-day notice period when they'll let you know in terms of timing from that to an Adcom. So I would assume at least could be, say, 3 to 6 months as a delay here. I'm not sure if you want to comment on those timing considerations. And I realize it's been a very short amount of time since you've had to digest this information, but any analog situations that you may have looked at or come aware of as it pertains to a novel mechanism and anything that might give you or us some sort of comfort as it pertains to this situation in general?

Enrique A. Conterno

CEO & Director

Yes. No. Thank you very much. We are, quite frankly, in unprecedented territory when it comes to having had an extension and then within the sanction period now, having an Adcom, clearly not a good situation from a timing perspective. We don't question the possibility or the wisdom of having an Adcom, in fact, we had very much shared that we were preparing for that back in the spring, but it -- an Adcom was not called. So now we find ourselves very late in the process. And at this point in time, we have to look forward to try to prepare, in the best way possible, to ensure that we can have the most successful Adcom possible and sharing all of our data and why we have the confidence that we have on roxadustat.

So I -- we will be looking, of course, at other types of examples and so forth and learning from that as part of the Adcom preparation. I don't know, Mark Eisner, if you want to add anything to what I said.

Mark Eisner

Chief Medical Officer

No, I think you summarized it well, Enrique. I mean we don't know the data, the Adcom yet. So it's difficult to speculate on the exact time frame, but we'll be preparing carefully. We'll be ready for the discussion. And we actually welcome the input from nephrologists and the external medical and scientific community, just the timing is surprising.

Operator

Next question comes from Yaron Werber from Cowen.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

So Enrique, I just have maybe a couple of questions. Number one, I was under the impression that the original NDA was sent to hematology. So is it that hematology asked cardiorenal for advice and the cardiorenal Adcom was called just so we -- it sounds like they didn't send the application across to a different division, but it sounds like they're calling an Adcom from another division and not totally surprising given that division has experience, at least with ESAs.

And then secondly, as you think about OpEx and for this year -- and I know you don't give guidance, but can you give us a little bit of a sense what's going on with -- IPF is a little slow because of COVID, but just a little bit, how do we think about OpEx?

Enrique A. Conterno

CEO & Director

Yes. So yes, your understanding is also the understanding that I had on both hematology and renal. They are both under the same overall leadership at FDA, but we were informed today that that cardiorenal would be the one basically conducting the Adcom or hosting the Adcom.

Sorry, I missed your -- the second part of your question was related to COVID. Were you asking about operating expenses?

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Exactly. Just -- some of the R&D would have been IPF-related, but that's slower to ramp. So just how do we think about the OpEx for the year overall and maybe a little bit of R&D?

Enrique A. Conterno

CEO & Director

Yes. We, of course, have -- are looking at our operating expenses. We do this as a matter of discipline. Whenever we had even the 3-month extension, I asked for an overall review of operating expenses. And given that we were going to be launching roxadustat later, now we need to undergo a similar process now that we have a further delay. So clearly, when it comes to pam, we're trying to enroll as quickly as we can, but we need to be thoughtful about every single expense here at FibroGen. We do have a good balance sheet and a good position, but we need to make sure that it's invested in the things that can add the most value at all times and continue to have operating discipline anytime things and some of the assumptions change.

Operator

Our next question comes from Andy Hsieh from William Blair.

Tsan-Yu Hsieh

William Blair & Company L.L.C., Research Division

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I'm just wondering, high level, heading into the Adcom, what's your confidence level, right? So basically, before it's kind of a two-party interaction between you and the FDA, the renal cardio division. And now they're bringing a third party, external experts, kind of democratizing the process. So maybe comment on the confidence level and the ability for you to kind of highlight the data in that avenue. And also for the preparation for incident dialysis, is that kind of a separate population that you would want to kind of single out during the presentation?

Enrique A. Conterno

CEO & Director

Yes. Clearly, I won't be sharing what are we planning to present and so forth, but you can imagine, of course, the data that we have on incident dialysis, we believe, is some of our strongest data. As we think about MACE and MACE+ significance in that population. So clearly, very, very important data. I -- what I would share, I think you talked about democratizing the processes, transparency. But I think it's also a good opportunity to get the external community, including nephrologists, patient advocates to opine about some of the needs out there. And I think, honestly, I think in that way, I think this -- the Adcom could be refreshing to be able to hear some of the interest that the clinical community has on the product.

That's what we hear, basically, whether it's at ASN, either directly shared comments, but also how you -- how interested people are in the different presentations that we had, whether were oral presentations or posters at ASN. So I look forward to the full engagement of the scientific community. So that's the perspective that I would provide.

Operator

Your next question comes from Paul Choi from Goldman Sachs.

Aliza Bram Seidenfeld

Goldman Sachs Group, Inc., Research Division

This is Aliza on for Paul. A quick one on the Adcom for us. It seems like previously the FDA was reviewing roxa in terms of both the DD and NDD populations together. With the new news on the Adcom, are you guys still expecting a similar review? Do you have any indication that the agency might review these populations and/or indications more separately? How you're thinking about that would be great.

Enrique A. Conterno

CEO & Director

Yes. I will have Mark Eisner maybe comment and respond to that question.

Mark Eisner

Chief Medical Officer

Yes. So it's a great question. Thank you. We can't really obviously share the details of the FDA's overall intent because we don't want to speculate. But we're very confident in our data for both populations. I mean the data are the same today as they were yesterday, and we had the FDA tell us today about the Adcom. So we continue to feel very confident in the data. And as Enrique said, I think it's actually, although the timing is unfortunate, it's a great opportunity to really hear from the community, whether they be patients and their advocates, nephrologists, so the clinicians about how important and innovative this product is and can be for patients. And there's been very little innovation in this space over the past 30 years for CKD anemia, and we really believe the roxadustat can provide really significant clinical benefit to patients in both populations. So we're looking forward to that discussion in the public venue.

Operator

Our next question comes from Difei Yang from Mizuho Securities.

Difei Yang

Mizuho Securities USA LLC, Research Division

So just 3 quick questions. One, I apologize if I missed that. Will you be -- are you expecting the 55-day prep time leading up to Adcom? Or will it be shortened in some fashion?

So then the second question is that, would you have the option to call back CMO for this Adcom? Or do you think she will not be there?

Then the third question is with regards to EMA, I think you have said you're still expecting decision midyear 2021. I'm wondering if you are able to give us a little bit more detail between now and approval, what other things needs to happen?

Enrique A. Conterno

CEO & Director

Yes. I'm going to have Mark Eisner respond to these questions, and I'll complement his answers.

Mark Eisner

Chief Medical Officer

Right. So in terms of your first question about the 55-day prep time, the FDA has not provided us a date for the advisory committee. And as soon as they do, we'll be able to communicate that, but we would assume that they're going to conform to their typical practices. In terms of calling back the CMO, Dr. Peony will continue to be working as a consultant for us for the next 6 months. So we'll have access to her expertise. And remember, the expertise on this product, although Dr. Yu is very expert, is deep and broad within both FibroGen and AstraZeneca. So we're very confident that we will be able to bring a very appropriate and invigorated discussion at the time of the Adcom. And then in terms of the EMA, yes, there's been no change to our expectations around the midyear approval for roxadustat in the European Union.

Operator

All right. At this time, I would like to turn it back to the speakers for further comments. I'm showing no further questions at this time. Please go ahead.

Enrique A. Conterno

CEO & Director

We appreciate everyone's participation in today's investor call and your interest in FIbroGen. Please follow up with our Investor Relations team if you have any questions we have not addressed on the call, and enjoy the rest of your day. Thank you.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for participating. You may now disconnect.

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2020

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT **OF 1934**

> For the transition period from to . Commission file number: 001-36740

FIBROGEN, INC.

(Exact name of registrant as specified in its charter)

Delaware

77-0357827

(State or other jurisdiction of incorporation or organization) 409 Illinois Street

(I.R.S. Employer Identification No.)

San Francisco, CA (Address of principal executive offices) 94158

(zip code)

Registrant's telephone number, including area code:

(415) 978-1200

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, \$0.01 par value	FGEN	The NASDAQ Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes 🗵 No 🗆

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes \square No \square

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☑ No □

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes $\ensuremath{\square}$ No $\ensuremath{\square}$

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the

Exchange Act: Large accelerated filer **√** Accelerated filer Non-accelerated filer П Smaller reporting company П Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. \square

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. 🗹 Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes \square No \square

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, computed by reference to the closing price as of the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2020, was approximately \$2,127.6 million. Shares of Common Stock held by each executive officer and director and stockholders known by the registrant to own 10% or more of the outstanding stock based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes

The number of shares of common stock outstanding as of January 31, 2021 was 91,560,468.

DOCUMENTS INCORPORATED BY REFERENCE

Items 10, 11, 12, 13 and 14 of Part III of this Annual Report on Form 10-K incorporate information by reference from the definitive proxy statement for the registrant's 2021 Annual Meeting of Stockholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A not later than after 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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FORWARD-LOOKING STATEMENTS

This Annual Report filed on Form 10-K and the information incorporated herein by reference, particularly in the sections captioned "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," contains forwardlooking statements, which involve substantial risks and uncertainties. In this Annual Report, all statements other than statements of historical or present facts contained in this Annual Report, including statements regarding our future financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "believe," "will," "may," "estimate," "continue," "anticipate," "contemplate," "intend," "target," "project," "should," "plan," "expect," "predict," "could," "potentially" or the negative of these terms or other similar terms or expressions that concern our expectations, strategy, plans or intentions. Forward-looking statements appear in a number of places throughout this Annual Report and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, our ongoing and planned preclinical development and clinical trials, the timing of and our ability to make regulatory filings and obtain and maintain regulatory approvals for roxadustat, pamrevlumab and our other product candidates, our intellectual property position, the potential safety, efficacy, reimbursement, convenience clinical and pharmaco-economic benefits of our product candidates, the potential markets for any of our product candidates, our ability to develop commercial functions, our ability to operate in China, expectations regarding clinical trial data, our results of operations, cash needs, spending of the proceeds from our initial public offering, financial condition, liquidity, prospects, growth and strategies, the industry in which we operate and the trends that may affect the industry or us. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions described in the section of this Annual Report captioned "Risk Factors" and elsewhere in this Annual Report. A summary of these risk factors can be found in the following section, however please refer to the full risk factors in Item 1A "Risk Factors". These risks are not exhaustive. Other sections of this Annual Report may include additional factors that could adversely impact our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. We cannot assure you that the events and circumstances reflected in the forward-looking statements will be achieved or occur. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. The forward-looking statements made in this Annual Report are based on circumstances as of the date on which the statements are made. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this Annual Report or to conform these statements to actual results or to changes in our expectations.

This Annual Report also contains market data, research, industry forecasts and other similar information obtained from or based on industry reports and publications, including information concerning our industry, our business, and the potential markets for our product candidates, including data regarding the estimated size and patient populations of those and related markets, their projected growth rates and the incidence of certain medical conditions, as well as physician and patient practices within the related markets. Such data and information involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.

You should read this Annual Report with the understanding that our actual future results, levels of activity, performance and achievements may be materially different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

SUMMARY RISK FACTOR

The success of the Company will depend on a number of factors, many of which are beyond our control and involve risks, including but not limited to the following:

Risks Related to the Development and Commercialization of Our Product Candidates

- We are substantially dependent on the success of our lead product, roxadustat, and our second compound in development, pamrevlumab.
- As a company, we have limited commercialization experience, and the time and resources to develop such experience are significant. If we fail to achieve and sustain commercial success for roxadustat with our collaboration partners, our business would be harmed.
- Although regulatory approval has been obtained for roxadustat in China, Japan, and Chile, we may be unable to obtain regulatory approval for other countries, or such approval may be delayed or limited, due to a number of factors, many of which are beyond our control.
- The results of the FDA Cardiovascular and Renal Drugs Advisory Committee meeting may affect roxadustat's approvability or label in CKD anemia.
- Preclinical, Phase 1 and Phase 2 clinical trial results may not be indicative of the results that may be obtained in larger clinical trials.
- We do not know whether our ongoing or planned clinical trials of roxadustat or pamrevlumab will need to be redesigned based on interim results or if we will be able to achieve sufficient patient enrollment or complete planned clinical trials on schedule.
- Our product candidates may cause or have attributed to them undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.
- · Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.
- If we or our manufacturers cannot properly manufacture sufficient product, we may experience delays in development, regulatory approval, launch or successful commercialization.
- Regulatory authorities will do their own benefit risk analysis and may reach a different conclusion than we or our partners have, and these regulatory authorities may base their approval decision on different analyses, data, and statistical methods than ours.
- Even if we are able to obtain regulatory approval of our product candidates, the label we obtain may limit the indicated uses for which our product candidates may be marketed.
- · We face substantial competition in the discovery, development and commercialization of product candidates.
- No or limited reimbursement or insurance coverage of our approved products, if any, by third-party payors may render our products less attractive to patients and healthcare providers.

Risks Related to Severe Acute Respiratory Syndrome Coronavirus 2 and the Resulting Coronavirus Disease ("COVID-19")

Our business could continue to be adversely affected by the ongoing COVID-19 global pandemic.

Risks Related to Our Reliance on Third Parties

- If our collaborations were terminated or if Astellas or AstraZeneca were to prioritize other initiatives over their collaborations with us, our ability to successfully develop and commercialize our product candidates would suffer.
- If our preclinical and clinical trial contractors do not properly perform their agreed upon obligations, we may not be able to obtain or may be delayed in receiving regulatory approvals for our product candidates.
- We currently rely, and expect to continue to rely, on third parties to conduct many aspects of our product manufacturing and distribution, and these third parties may terminate these agreements or not perform satisfactorily.
- Certain components of our products are acquired from single-source suppliers or without long-term supply agreements. The loss of these suppliers, or their failure to supply, would materially and adversely affect our business.

Risks Related to Our Intellectual Property

- · If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.
- · Intellectual property disputes may be costly, time consuming, and may negatively affect our competitive position.
- Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the
 possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.
- The cost of maintaining our patent protection is high and requires continuous review and diligence. We may not be able to effectively
 maintain our intellectual property position throughout the major markets of the world.
- The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the U.S., and we may encounter significant problems in securing and defending our intellectual property rights outside the U.S.
- Intellectual property rights do not address all potential threats to any competitive advantage we may have.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a
material adverse effect on our business, operations and prospects.

Risks Related to Government Regulation

- The regulatory approval process is highly uncertain and we may not obtain regulatory approval for our product candidates.
- Our product candidates could fail to receive regulatory approval from the FDA or other regulatory authorities.
- Our current and future relationships with customers, physicians, and third-party payors are subject to healthcare fraud and abuse laws, false
 claims laws, transparency laws, privacy and security laws, and other regulations. If we are unable to comply with such laws, we could face
 substantial penalties.
- We are subject to laws and regulations governing corruption, which will require us to maintain costly compliance programs.
- We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these, or if we otherwise fail to maintain an effective system of internal control, it may result in material misstatements in our financial statements.
- The impact of recent U.S. healthcare reform, its potential partial or full repeal, and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.
- Roxadustat is considered a Class 2 substance on the 2019 World Anti-Doping Agency Prohibited List that could limit sales and increase security and distribution costs for our partners and us.
- · Our employees may engage in misconduct or improper activities, which could result in significant liability or harm our reputation.
- · If we fail to comply with environmental, health or safety laws and regulations, we could incur fines, penalties or other costs.

Risks Related to Our International Operations

- We have established operations in China and are seeking approval to commercialize our product candidates outside of the U.S., and a number of risks associated with international operations could materially and adversely affect our business.
- · The pharmaceutical industry in China is highly regulated and such regulations are subject to change.
- We have limited experience distributing drugs in China.
- We use our own manufacturing facilities in China to produce roxadustat API and drug product. There are risks inherent to operating
 commercial manufacturing facilities, and with these being our single source suppliers, we may not be able to continually meet market
 demand
- As a company, we have limited experience in pharmacovigilance, medical affairs, and management of the third-party distribution logistics, and cannot assure you we will be able to meet regulatory requirements or operate in these capacities successfully.
- We and our collaboration partner in China, AstraZeneca, may experience difficulties in successfully growing and sustaining sales of roxadustat in China.
- · The retail prices of any product candidates that we develop may be subject to pricing control in China and elsewhere.
- FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.
- Any capital contributions from us to FibroGen Beijing must be approved by the Ministry of Commerce in China, and failure to obtain such
 approval may materially and adversely affect the liquidity position of FibroGen Beijing.
- We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.
- Because FibroGen Beijing's funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen Beijing
 deposits its funds could adversely affect our business.
- We may be subject to tax inefficiencies associated with our offshore corporate structure.
- Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.
- Uncertainties with respect to the China legal system could have a material adverse effect on us.
- Changes in China's economic, governmental, or social conditions could have a material adverse effect on our business.
- Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may
 materially and adversely affect our business, financial condition and results of operations.

Risks Related to the Operation of Our Business

Please see below for additional risk factors related to the operation of our Business.

There are also a variety of Risks Related to Our Common Stock

• Please see below for additional risk factors to our Common Stock.

PARTI

ITEM 1. BUSINESS

OVERVIEW

We are a leading biopharmaceutical company discovering, developing and commercializing a pipeline of first-in-class therapeutics. We apply our pioneering expertise in hypoxia-inducible factor ("HIF") biology, 2-oxoglutarate enzymology, and connective tissue growth factor ("CTGF") biology to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer.

Roxadustat, our most advanced product, is an oral small molecule inhibitor of HIF-prolyl hydroxylase ("HIF-PH") activity that acts by stimulating the body's natural pathway of erythropoiesis, or red blood cell production.

We and our collaboration partner AstraZeneca AB ("AstraZeneca") continue to expand the commercialization of roxadustat (tradename: 爱瑞卓®) in the People's Republic of China ("China") where it is approved for the treatment of anemia caused by chronic kidney disease ("CKD") in non-dialysis and dialysis patients. Roxadustat was added to the National Reimbursement Drug List ("NRDL"), effective January 1, 2020. As of the end of 2020, roxadustat was listed at hospitals that represent approximately 70% of the CKD anemia market opportunity in China and we continue to focus on adding additional temporary and permanent hospital listings for roxadustat.

In Japan, our partner Astellas Pharma Inc. ("Astellas") continues the commercial launch of EVRENZO® (roxadustat). Astellas received approval of the supplemental New Drug Application ("NDA") for the use of EVRENZO in patients with anemia of CKD not on dialysis from the Pharmaceuticals and Medical Devices Agency in November 2020, and it is now approved for the treatment of anemia associated with CKD in both non-dialysis and dialysis patients.

With respect to our United States ("U.S.") NDA for roxadustat for the treatment of anemia due to CKD submitted for review in December 2019 to the U.S. Food and Drug Administration ("FDA"), in December 2020, the FDA extended the review period of the NDA by three months for FibroGen to submit additional analyses of existing roxadustat clinical data, and set a new Prescription Drug User Fee Act ("PDUFA") goal date of March 20, 2021. On March 1, 2021, the FDA informed us that the Cardiovascular and Renal Drugs Advisory Committee will hold an advisory committee meeting to review the NDA for roxadustat. The date of the advisory committee meeting has not been set. As a result of this communication, we will not receive an approval decision by the PDUFA goal date.

In May 2020, the Marketing Authorization Application ("MAA") for roxadustat for the treatment of anemia in patients with CKD, submitted by our partner Astellas, was accepted for regulatory review by the European Medicines Agency ("EMA"). Astellas expects an approval decision mid-2021.

EVRENZO® (roxadustat) has also been approved for the treatment of anemia in CKD patients on dialysis and patients not on dialysis in Chile. In collaboration with AstraZeneca, applications for marketing approval of roxadustat in CKD anemia have been submitted in Canada, Australia, Mexico, Brazil, Taiwan, South Korea, Philippines, Singapore, India, Colombia, and Thailand.

Beyond anemia in CKD, roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes ("MDS").

We have completed enrollment in our Phase 2 clinical trial of roxadustat in the U.S. in chemotherapy-induced anemia ("CIA"), and we expect topline data from this study in the second half of 2021.

Pamrevlumab is our first-in-class antibody developed to inhibit the activity of CTGF, a common factor in fibrotic and proliferative disorders characterized by persistent and excessive scarring that can lead to organ dysfunction and failure. Pamrevlumab is in Phase 3 clinical development for the treatment of idiopathic pulmonary fibrosis ("IPF"), locally advanced unresectable pancreatic cancer ("LAPC"), and Duchenne muscular dystrophy ("DMD").

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE

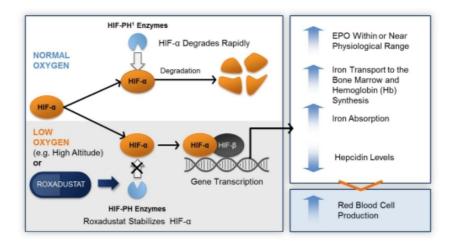
In collaboration with our partners AstraZeneca and Astellas, we have completed 16 Phase 3 studies worldwide in over 11,000 patients to support our regulatory filings in the U.S., Europe, China, and Japan.

After describing the mechanism of action of roxadustat, which is the first in a new class of potential anemia drugs, we provide some background on the CKD anemia market and a summary of our Phase 3 program along with some of the most important results.

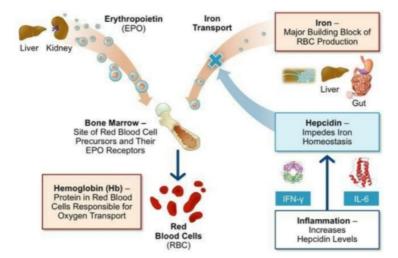
Roxadustat Mechanism of Action

Roxadustat is an orally administered reversible inhibitor of HIF-PH. Inhibition of prolyl hydroxylase stabilizes HIF, which stimulates a coordinated erythropoietic response that includes the increase of plasma endogenous erythropoietin ("EPO") levels and reduction of hepcidin, a key regulator of iron homeostasis. In healthy individuals under normal oxygen conditions, HIF-PH tags HIF-alpha for degradation and the HIF pathway is not activated. However, under low oxygen conditions, the HIF-PH enzymes cannot function and HIF-alpha accumulates. HIF-alpha then combines with HIF-beta, and the newly formed HIF complex initiates transcription of a number of genes involved in the erythropoietic process, which ultimately leads to increased oxygen delivery to tissues.

In anemia of CKD, roxadustat temporarily inhibits HIF-PH, preventing degradation of HIF-alpha and activating the HIF pathway, which stimulates a coordinated erythropoietic response that includes EPO production and the reduction of hepcidin.



The coordinated erythropoiesis activated by roxadustat includes both the stimulation of erythroid maturation, by increasing the body's production of EPO, and an increase in iron availability for hemoglobin synthesis in part through a decrease in hepcidin levels, which is particularly important in patients with inflammation. Patients taking roxadustat typically have a transient increase in circulating endogenous EPO levels at peak concentration within or near the physiologic range naturally experienced by humans adapting to hypoxic conditions such as at high altitude, following blood donation, or impaired lung function, such as pulmonary edema.



By contrast, erythropoiesis stimulating agents ("ESAs") act only to stimulate erythroid maturation without a corresponding increase in iron availability, and are typically dosed at well above the natural physiologic range of EPO. The sudden demand for iron stimulated by ESA-induced erythropoiesis can lead to functional or absolute iron deficiency. We believe these high doses of ESAs are a main cause of the significant safety issues that have been attributed to this class of drugs. In addition, the lack of a coordinated increase in iron availability with ESAs may explain the hyporesponsiveness of patients with inflammation to this class of drugs. It also explains why patients taking ESAs need more IV iron supplementation and red blood cell transfusions than patients taking roxadustat do. Not only are IV iron and blood transfusions more costly than oral iron, but both are also associated with increased risk of hospitalization and death.

The differentiated mechanism of action of roxadustat, which involves induction of the body's own natural pathways to achieve a more complete erythropoiesis, has the potential to provide a safe and effective treatment for anemia, including in the presence of inflammation, which normally limits iron availability.

Background of Anemia in Chronic Kidney Disease

Chronic kidney disease is a progressive disease characterized by gradual loss of kidney function that may eventually lead to kidney failure or end-stage renal disease requiring dialysis or a kidney transplant to survive. CKD affects 12% to 14% of the global adult population. CKD is more prevalent in developed countries but is also growing rapidly in emerging markets such as China.

Anemia is a complication of CKD and can be a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, a protein in red blood cells that carries oxygen to cells throughout the body. Anemia becomes increasingly common as kidney function declines and is associated with increased risk of hospitalization, cardiovascular complications and death, and frequently causes significant fatigue, cognitive dysfunction, and considerable reduction of quality of life.

There are approximately 39 million 1 CKD patients in the U.S., an estimated 6 million of whom have an mia 2 .

When ESAs were introduced in 1989, they dramatically reduced the need for blood transfusions in CKD patients, which was a material development since transfusions reduce the patient's opportunity for a kidney transplant and increase the risk of infections and complications such as heart failure and allergic reactions. However, multiple randomized clinical trials with ESAs suggested safety risks of ESA therapies, and as a result, the anemia guidelines and approved labels have changed to more restrictive use of ESAs.

Bikbov B et al. "Global regional and national burden of chronic kidney disease 1990-2017 - a systematic analysis for the Global Burden of Disease Study 2017." The Lancet, 395 (2020): 709-33. Web. 13 Feb. 2020.

2Based on 15.4% of CKD patients having anemia, (where anemia is defined as hemoglobin levels of \leq 12 g/dL in women and \leq 13 g/dL in men.

In the dialysis-dependent population, most patients start receiving ESAs when the patient is transitioning to dialysis care. As of the end of 2018, there were over 550,000 CKD patients on dialysis in the U.S., a large majority of whom required anemia therapy.

There were approximately 127,000 incident dialysis patients in 2018. Despite the higher risk of blood transfusions, cardiovascular events, and hospitalization in patients with anemia, only 14.6% of patients in 2018 were treated with ESAs prior to initiating dialysis notwithstanding a mean hemoglobin level of 9.3 g/dL at the time of dialysis initiation.

These treatment figures at the time of dialysis initiation demonstrate how undertreated CKD anemia is currently in non-dialysis patients. However, we believe there will be approximately 2 million addressable non-dialysis CKD anemia patients in the U.S. annually, based on the hemoglobin entry criteria in our Phase 3 clinical trials recommending initiation of treatment when a patient's hemoglobin level is less than 10 g/dL. In addition to the safety concerns raised for ESAs, which may have been a greater impediment to treatment in the non-dialysis setting, other factors which contribute to the recent historical under-treatment of anemia in non-dialysis patients are related to the form of administration and accessibility of ESA products. ESAs are typically administered by subcutaneous injections, which is more difficult outside of dialysis centers or nephrology practices where non-dialysis patients are typically treated.

Number of Patients

Roxadustat Phase 3 CKD Anemia Clinical Program

Study Sponsor, Number	Comparator	U.S.	Europe	China	Japan
NON-DIALYSIS					
FibroGen - FGCL-4592-060 (ANDES)	Placebo	922			
Astellas - 1517-CL-0608 (ALPS)	Placebo	59	7		
AstraZeneca - D5740C00001 (OLYMPUS)	Placebo	2,7	81		
Astellas - 1517-CL-0610	Darbepoetin alfa		616		
FibroGen - FGCL-4592-808	Placebo			151	
Astellas - 1517-CL-0310	Darbepoetin alfa				334
Astellas - 1517-CL-0314	None				99
Non-Dialysis-Dependent CKD Subtotal					
by Region		4,300	4,916	151	433
STABLE DIALYSIS					
Astellas - 1517-CL-0613 (PYRENEES)	Epoetin alfa or				
	Darbepoetin alfa		838		
FibroGen - FGCL-4592-806	Epoetin alfa			304	
Astellas - 1517-CL-0302	None				56
Astellas - 1517-CL-0307	Darbepoetin alfa				303
Astellas - 1517-CL-0308	None				75
Astellas - 1517-CL-0312	None				164
STABLE AND INCIDENT DIALYSIS					
AstraZeneca - D5740C00002 (ROCKIES)	Epoetin alfa	2,133			
FibroGen - FGCL-4592-064 (SIERRAS)	Epoetin alfa	741			
INCIDENT DIALYSIS					
FibroGen - FGCL-4592-063 (HIMALAYAS)	Epoetin alfa	1,043			
Dialysis-Dependent-CKD Subtotal by					
Region		3,917	4,755	304	598
Total by Regulatory Approval Region		8,217	9,671	455	1,031
Combined Total to Support U.S. and Europe					
Approvals		9,6	71		

The primary efficacy endpoint was met in each of the pivotal studies for the U.S. NDA and Europe MAA, as shown below:

Summary of Results from Individual Phase 3 Studies of Roxadustat in CKD Anemia

Summary of Roxadustat U.S. and Europe Phase 3 Primary Efficacy Results

		Endpoint		Endpoint	
Study Sponsor, Number	U.S. Primary Endpoint	Met	Europe Primary Endpoint	Met	
NON-DIALYSIS					
FibroGen - FGCL-4592-060 (ANDES)	Superior to Placebo (p<0.0001)	✓	Superior to Placebo (p<0.0001)	✓	
Astellas - 1517-CL-0608 (ALPS)	Superior to Placebo (p<0.001)	\checkmark	Superior to Placebo (p<0.001)	✓	
AstraZeneca - D5740C00001 (OLYMPUS)	Statistically-Significant Improvement in Hb Change Compared to Placebo	✓	Statistically-Significant Improvement in Hb Change Compared to Placebo	1	
STABLE DIALYSIS					
Astellas - 1517-CL-0613 (PYRENEES)	Non-Inferior to ESAs	✓	Non-Inferior to ESAs	✓	
STABLE AND INCIDENT					
DIALYSIS					
AstraZeneca - D5740C00002 (ROCKIES)	Statistically-Significant Larger Hb Increase Compared to Epoetin Alfa	✓	Statistically-Significant Larger Hb Increase Compared to Epoetin Alfa	1	
FibroGen - FGCL-4592-064 (SIERRAS)	Superior to Epoetin Alfa (p<0.0001)	✓	Superior to Epoetin Alfa (p<0.0001)	✓	
INCIDENT DIALYSIS					
FibroGen - FGCL-4592-063 (HIMALAYAS)	Superior to Epoetin Alfa (p=0.0005)	✓	Non-Inferior to Epoetin Alfa	✓	

Additional Highlights from Recent Publications and Presentations of Roxadustat in CKD Anemia

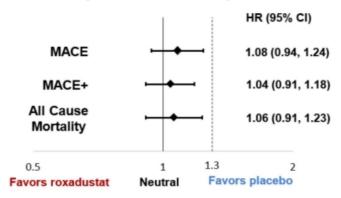
Pooled Cardiovascular Safety Results

In the U.S., the primary safety endpoint is time to first major adverse cardiovascular event ("MACE"), a composite endpoint of all-cause mortality, stroke and myocardial infarction, with secondary safety endpoint of "MACE+", a composite endpoint consisting of the three components in MACE plus heart failure or unstable angina requiring hospitalization. The below cardiovascular safety analyses reflect the pooling strategy and analytical approach that was agreed upon with the FDA and presented in scientific journals/professional meetings.

Non-Dialysis - Pooled Cardiovascular Safety Data

The intent-to-treat analyses, inclusive of data during on-treatment and post treatment long term follow-up (until a common study end date), was used in our primary cardiovascular safety analysis method for non-dialysis in the U.S. This approach accounts for the higher drop-out rate in the placebo arm. The figure below shows that in the 4,270 pooled non-dialysis patients (OLYMPUS, ANDES, and ALPS), the risk of MACE, MACE+, and all-cause mortality in roxadustat patients were comparable to that in placebo patients based on a reference non-inferiority margin of 1.3.

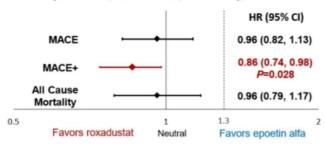
Time to event endpoints using Cox model, ITT analysis NDD (OLYMPUS, ANDES, ALPS), N=4270



Dialysis - Pooled Cardiovascular Safety Data

In the pooled on-treatment analysis of 3,880 dialysis patients (HIMALAYAS, SIERRAS, and ROCKIES), the risk of MACE and all-cause mortality in roxadustat patients were comparable to epoetin alfa, based on a reference non-inferiority margin of 1.3. Roxadustat lowered the risk of MACE+ by 14% compared to epoetin alfa based on a hazard ratio of 0.86 and an upper bound of 95% CI under 1.0. The hazard ratios represent a point estimate of relative risk.

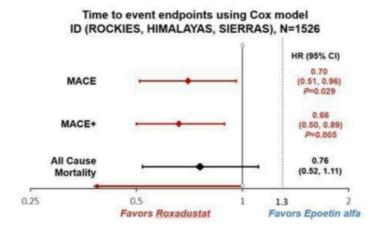
Time to event endpoints using Cox model DE (ROCKIES, HIMALAYAS, SIERRAS), N=3880



Incident Dialysis Subgroup - Pooled Cardiovascular Safety Data

Data from the pooled incident dialysis patients were recently published in Kidney International Reports. (Provenzano R et al. Pooled Analysis of Roxadustat for Anemia in Patients with Kidney Failure Incident to Dialysis. KI Reports 2021. Available at https://www.kireports.org/article/S2468-0249(20)31851-9/fulltext. Accessed on 11FEB2021.)

This is a clinically important subgroup of dialysis patients who started participation in roxadustat Phase 3 studies within their first four months of dialysis initiation. In these 1,526 incident dialysis patients, roxadustat reduced the risk of MACE by 30% and MACE+ by 34%, with a trend towards lower all-cause mortality. The lower MACE and MACE+ risks (compared to epoetin alfa) are based on hazard ratios of 0.70 and 0.66, respectively, with the upper bound of 95% CI under 1.0 for both endpoints. We believe this incident dialysis subpopulation provides clinically and commercially relevant and generalizable results for comparison of roxadustat versus epoetin alfa because most incident dialysis patients (as opposed to stable dialysis patients) were ESA-naïve or had only limited exposure to ESAs prior to study entry. In addition, the initiation of anemia therapy in this incident dialysis subgroup resembles clinical practice as the vast majority of U.S. patients start anemia therapy early in dialysis treatment (during the first four months of treatment).



Iron-Metabolism Data

In non-dialysis patients, roxadustat was effective regardless of whether the "iron-repletion" criteria (ferritin >=100 ng/mL AND TSAT >=20%) were met, including the 40% of patients whose iron stores were below those required for ESA treatment. Roxadustat also increased both serum iron and transferrin, resulting in the long-term clinical stability of TSAT while increasing the absolute amount of iron available for erythropoiesis.

In dialysis patients, roxadustat treated patients required less IV iron supplementation than patients treated with ESA. Roxadustat facilitated iron transport and utilization by increasing both serum iron and iron-carrying capacity (TIBC), whereas these parameters were decreased and unchanged, respectively, with epoetin alfa. We believe these changes were most likely driven by the downstream effects of reduced hepcidin in roxadustat treated patients.

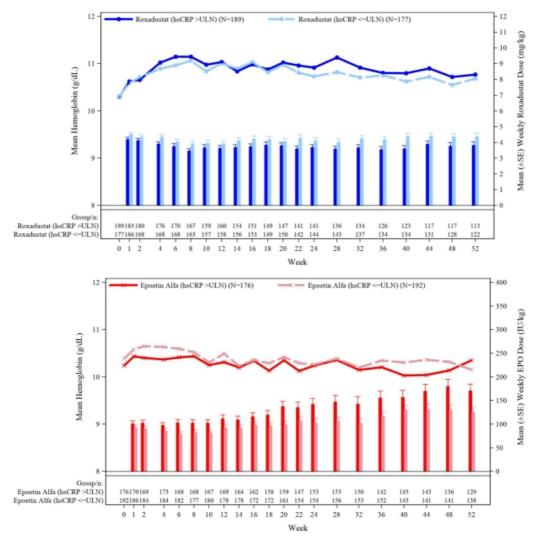
Efficacy at Raising Hemoglobin Irrespective of Iron Replete Status

In the non-dialysis pool (4,277 patients from ANDES, OLYMPUS, and ALPS), roxadustat increased hemoglobin (by 1.94 g/dL) regardless of whether patients were iron-replete (patients shown to have sufficient baseline stores of iron in their body, TSAT \geq 20% and Ferritin \geq 100 ng/mL) or not iron-replete.

Sierras - U.S. Only Dialysis Study

In the U.S. dialysis study SIERRAS, roxadustat raised and maintained Hb levels with stable mean doses over time regardless of baseline inflammation status, as measured by CRP levels. The dose requirement of roxadustat was not impacted by inflammation.

Mean Hb and Mean Weekly Dose of roxadustat (Top Figure) and Epoetin Alfa (Bottom Figure) Over Time in Patients with hsCRP ≤ULN or >ULN (SIERRAS)



hsCRP: high-sensitivity C-reactive protein; SE: standard error; ULN: upper limit of normal.

The proportion of patients who required at least one red blood cell transfusion in the first 52 weeks was 12.5% with roxadustat compared to 21.1% with epoetin alfa (p<0.05) in SIERRAS.

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE IN CHINA

In August 2019, roxadustat (China tradename: 爱瑞卓®) received marketing authorization in China for the treatment of anemia caused by CKD in non-dialysis-dependent patients. Treatment for anemia caused by CKD in dialysis-dependent patients was approved in December 2018.

In July 2019, results from our two China Phase 3 clinical trials were published in the New England Journal of Medicine.3 4

In December 2019, roxadustat was included on the updated NRDL released by China's National Healthcare Security Administration. Roxadustat is included on the NRDL for the treatment of anemia in CKD.

Market Opportunity

The currently available forms of treatment in China for anemia in CKD include ESAs, oral iron, intravenous iron, traditional Chinese medicine, and combinations thereof. ESAs are the largest segment, which we estimate to be approximately \$275 million in sales, or approximately 80% of the total ESA market based on data from IQVIA China Hospital Pharmaceutical Audit. With the unique benefits of roxadustat to treat previously unaddressable patient populations, we believe the overall CKD anemia market will increase.

China is experiencing epidemiological changes in metabolic diseases due to economic development, urbanization and an aging population. Diabetes and hypertension are the leading causes of CKD in China, and rates have been growing over past two decades. We believe the increase in diabetes and hypertension prevalence will result in an increase of CKD anemia patients.

Dialysis-Dependent CKD

Based on the latest estimates and published data, we believe there are over 600,000 dialysis patients in China, making it the largest single-country dialysis population in the world. With the substantial growth rate of dialysis patients (over 10% per year from 2011 to 2017), the Ministry of Health and the Chinese Society of Nephrology have publicly recognized the need for further investment in dialysis infrastructure.

The prevalence of CKD dialysis patients that have anemia (defined as hemoglobin < 10g/dL) is estimated to be over 90%.

Dialysis treatment is delivered in the form of hemodialysis or peritoneal dialysis. In China, approximately 85% of dialysis patients with CKD are on hemodialysis. Hemodialysis is performed primarily in dialysis clinics within hospitals, most of which are publicly owned. This is in contrast to the U.S. where freestanding dialysis centers located outside of hospitals is common practice. With recent regulatory changes, the number of privately owned dialysis clinics is growing at a rapid pace, a trend that has provided additional capacity to meet the growing demand. The remaining 14-15% of CKD patients (approximately 100,000) are on peritoneal dialysis, which is self-administered at home by patients, a setting which roxadustat is particularly well-suited for due to its oral administration. Peritoneal dialysis patients typically visit their nephrologists on a monthly basis at the hospital for monitoring and follow-up.

³N. Chen, et al. "Roxadustat Treatment for Anemia in Patients Undergoing Long-Term Dialysis" N Engl J Med 381 (2019): 1011-22. DOI: 10.1056/NEJMoa1901713

4N. Chen, et al. "Roxadustat for Anemia in Patients with Kidney Disease Not Receiving Dialysis" N Engl J Med 381 (2019): 1001-1010. DOI: 10.1056/NEJMoa1813599

Non-Dialysis-Dependent CKD

We estimate that there are over 10 million Stage 3-5 non-dialysis CKD patients in China with anemia (defined as hemoglobin < 10g/dL). We believe the addressable population of non-dialysis patients with anemia (anemic patients that have been diagnosed and treated for CKD) is approximately 2-3 million, with 1-2 million of these addressable patients in Stages 3 and 4 and 1 million in Stage 5 non-dialysis. This Stage 5 population that is dialysis-eligible but not receiving dialysis is characteristic of developing markets like China, and presents a particular opportunity for roxadustat, as many patients have severe anemia.

Unmet Medical Need and Roxadustat Differentiation in China

We believe there is a particularly significant unmet medical need for the treatment of anemia in CKD in China. Anemia is considered a risk multiplier for CKD patients and is commonly associated with increased rates of cardiovascular events, hospitalizations, CKD progression, and death. Several of the advantages that roxadustat, as an oral therapeutic, potentially offers over ESAs are particularly suited to address the unmet medical need in each of the three categories of CKD patients in China.

We believe there is chronic under-treatment of anemia within the CKD patient population on dialysis in China due in part to under-prescription of IV iron (often necessary for ESA treatment), and lack of efficacy in patients with inflammation. The most recent treatment guidelines published by the Chinese Society of Nephrology in 2018 recommended treatment to hemoglobin 11.0 g/dL to 12.0 g/dL. Even though over 70% of hemodialysis CKD patients, and approximately 60% of peritoneal dialysis CKD patients are treated with ESAs, based on the Chinese Renal Data System in 2015, less than 60% of dialysis patients reached 10.2 g/dL.

In the non-dialysis population and peritoneal dialysis population, only a small percentage of patients receive anemia treatment, and those who do, they receive only a minimal level of treatment, including patients who are eligible for dialysis and who have severe anemia. Roxadustat, as an oral medication, can be easily administered in any setting and stored at room temperature. Injectable drugs like ESAs present a challenge in China because even subcutaneous administration is performed at hospitals and not in the home, in part due to the difficulty in refrigeration and administration of injectable medicines. Frequent hospital visits, for the sole purpose of receiving injectable ESA treatment (as well as IV iron, which is often necessary with ESA treatment), can present a substantial logistical and financial burden to patients.

In the context of the rapidly growing China pharmaceutical market, we believe that the demand for anemia therapy will continue to grow as a result of an expanding CKD population, as well as the central government's mandate to make dialysis more available through government reimbursement and build-out of dialysis facilities. In addition, as the standard of living improves in China, the demand for access to innovative drugs increases. In this context, we believe that roxadustat is a particularly promising product for this market.

Commercialization

AstraZeneca is our commercialization partner for roxadustat in China. Under our collaboration agreement, AstraZeneca leads commercialization activities and has responsibility for sales and marketing, and market access. FibroGen has responsibility for medical affairs, manufacturing (as the Marketing Authorization Holder), and pharmacovigilance.

Pricing and Reimbursement

In December 2019, roxadustat was included for the treatment of anemia in CKD on the updated NRDL released by China's National Healthcare Security Administration. The list is effective for a standard two-year period from January 1, 2020 to December 31, 2021. Roxadustat will be subject to price re-negotiation at the end of 2021.

We believe reimbursement is one of the two most critical market access factors for commercialization success in China, with the other being hospital listings. China is mostly a single-payor market with near universal healthcare provided by the government. Over 95% of the population receives healthcare coverage under one government-funded medical reimbursement plan or another, each with different levels of reimbursement. Commercial health insurance is available but is minimally adopted, and is seen as a supplement above and beyond government reimbursement.

Reimbursement for roxadustat will differ based on multiple factors including the CKD patient population (dialysis vs. non-dialysis), location, patient employment status, and if roxadustat is qualified into the "Critical Disease" or "Chronic Disease" insurance programs for such locations. We expect roxadustat reimbursement rates will be largely consistent with those ESAs listed on the NRDL. We believe in the next few years and in many parts of the country, reimbursement will reach a level where patient out-of-pocket costs will be in the range of 10-20% for dialysis and 30-50% for non-dialysis.

Hospital Listing

Before roxadustat can be prescribed at a government hospital, which is 90% of the market in China, it has to be carried in the hospital formulary. The process of entry into the formulary is commonly referred to as "hospital listing". Decisions are made on a hospital-by-hospital basis, where hospital listing committees meet anywhere from every six months to every five years. Temporary listings can be used in the interim, where the head of the department could place an ad-hoc order with the formulary for a single or handful of patients for small quantities of roxadustat. These market access constraints impact all drugs, not just roxadustat. Consistent with the experience of other product launches in China, significant market uptake is usually seen a few years after launch, although in the case of roxadustat, it could be sooner given the inclusion in NRDL within 12 months of market approval.

Tendering

Tendering is a provincial level procedure. For drugs with multiple brands, it is a collective tender process for purchases by government hospitals of a medicine included in provincial or local medicine procurement catalogs. In the case of roxadustat, it is a more administrative process than for most drugs as roxadustat is currently the only drug of its class (HIF-PHI) available on the market. The tendering process of roxadustat is substantially complete in all 31 provinces in China.

ROXADUSTAT FOR THE TREATMENT OF ANEMIA IN CHRONIC KIDNEY DISEASE IN JAPAN

In Japan, our partner Astellas continues the commercial launch of EVRENZO® (roxadustat), targeting healthcare providers that care for approximately 330,000 dialysis patients across Japan. EVRENZO is now approved for the treatment of anemia associated with CKD in both non-dialysis and dialysis patients. The supplemental NDA for the use of roxadustat in patients with anemia of CKD not on dialysis was approved in November 2020 by the Pharmaceuticals and Medical Devices Agency.

In addition, the 14-day Prescription Rule that is typically in place for the first 12 months of a product's availability in Japan was lifted in December of 2020, creating a potential catalyst for EVRENZO utilization given it is the first HIF-PH inhibitor to no longer have this limitation.

ROXADUSTAT FOR THE TREATMENT OF CHEMOTHERAPY-INDUCED ANEMIA AND ANEMIA ASSOCIATED WITH MYELODYSPLASTIC SYNDROMES

Based on roxadustat's mechanism of action and safety and efficacy profile to date, we believe it has the potential to treat anemia associated with many other conditions, including CIA and MDS.

Background of Chemotherapy-Induced Anemia

As blood cell production in bone marrow is highly prolific, it is particularly vulnerable to the cytotoxic effects of chemotherapy used to treat cancer patients. Many chemotherapy agents directly impair hematopoiesis in bone marrow, including disruption of red blood cell production. The nephrotoxic effects of some cytotoxic agents, such as platinum-containing agents, can also result in decreased production of erythropoietin by the kidneys, further contributing to reduced red blood cell production. Radiation therapy has also been associated with hematologic toxicity.

Approximately 40% of total solid tumor cancer patients, or approximately 6.8 million people, undergo chemotherapy each year globally, including 1.7 million in the U.S. and 3.2 million in China. Between 60% and 80% of these patients develop anemia. The incidence and severity of CIA depend on a variety of factors, including the tumor type or the level of toxicity of the therapy, and further increases with each successive chemotherapy round. We believe the addressable population is approximately 600,000 in the U.S. and 500,000 in China.

ESAs have been recommended for patients experiencing CIA with the desirable goals of improvement in anemia-related symptoms and the avoidance of blood transfusion, which increases risk of infections and the risk of complications such as heart failure and allergic reactions. However, not all CIA patients respond to ESA therapy, which may be due to the etiology of their CIA or inflammatory comorbidity. ESA use also has associated toxicities, including increased thrombotic events, possible decreased survival and accelerated tumor progression, as published from randomized clinical trials and meta-analyses, that led to label restrictions and boxed warnings for ESAs in cancer populations in 2007, followed by the ESA Risk Evaluation and Mitigation Strategy ("REMS") program.

Market Opportunity for Roxadustat in Chemotherapy-Induced Anemia

ESA sales for CIA dropped significantly in the U.S. since the reported safety risks of ESA use in cancer patients in 2006, from estimated \$2.5 billion in 2006 to less than \$0.5 billion in 2019. During the same period, the prevalence of diagnosed CIA remained at similar levels, and is expected to grow slightly.

We believe that if our clinical program shows an acceptable safety and efficacy profile, roxadustat would have the potential to address anemia in this population of patients undergoing chemotherapy.

Clinical Development of Roxadustat in Chemotherapy-Induced Anemia

We have completed enrollment in WHITNEY, our Phase 2 clinical trial of roxadustat in the U.S. in CIA. This is a single-arm open label study investigating the efficacy and safety of roxadustat for the treatment of anemia in 92 patients receiving myelosuppressive chemotherapy treatment for non-myeloid malignancies, with a treatment duration of 16 weeks. We expect topline data from this study in the second half of 2021.

Background of Anemia in Myelodysplastic Syndromes

Myelodysplastic syndromes are a diverse group of bone marrow disorders characterized by ineffective production of healthy blood cells and premature destruction of blood cells in the bone marrow, leading to anemia. In most MDS patients, the cause of the disease is unknown.

The prevalence of MDS in the U.S. is estimated to be between 60,000 and 170,000, and continues to rise as more therapies become available and patients are living longer with MDS. Annual incidence rates are estimated to be 4.9/100,000 adults in the U.S., and 1.51/100,000 adults in China.

Anemia is the most common clinical presentation in MDS, seen in approximately 80% of MDS patients, and producing symptoms, including fatigue, weakness, exercise intolerance, shortness of breath, dizziness, and cognitive impairment.

Limitations of the Current Standard of Care for Anemia in Myelodysplastic Syndromes

Stem cell transplant is the only potentially curative therapy for MDS, but it is not feasible in most patients due to their advanced age and frailty. The high rate of severe anemia leaves recurring red blood cell transfusions as the mainstay of care in MDS patients. Transfusion can result in direct organ damage through transfusional iron overload. Transfusion dependent MDS patients suffer higher rates of cardiac events, infections and transformation to acute leukemia, and a decreased overall survival rate when compared with non-transfused patients with MDS, and decreased survival compared to an age-matched elderly population. Patients receiving red blood cell transfusions may require an iron chelator in order to address toxic elements of iron overload such as lipid peroxidation and cell membrane, protein, DNA, and organ damage.

Lower-risk MDS patients represent approximately 77% of total diagnosed MDS population. Most national and international guidelines recommend use of ESAs for anemia only in lower-risk MDS patients presenting with symptomatic anemia with serum EPO levels at or below 500 mU/mL.

Even among the eligible subpopulation, the effectiveness of ESAs in treating anemia in MDS remains limited, with the best clinical study results showing 40% to 60% erythroid response rates, in studies where significantly high doses of ESAs were used, enrolled patients had low serum EPO levels, and in lower-risk categories. New strategies to broaden the eligible population, improve anemia and maintain adequate iron balance, as well as avoidance of transfusions, are highly desired in managing patients with MDS.

Reblozyl® (luspatercept) was approved by the FDA in April 2020 for the treatment of anemia in adults with MDS with ring sideroblasts or myelodysplastic/myeloproliferative neoplasms with ring sideroblasts and thrombocytosis who need regular red blood cell transfusions and have not responded well to or cannot receive an ESA. It is the first and only erythroid maturation agent approved in the U.S., Europe, and Canada and is part of a global collaboration between Acceleron Pharma, Inc. and Bristol Myers Squibb. In 2020, Reblozyl net revenue was \$274 million, including \$115 million in Q4 2020.

Market Opportunity for Roxadustat in Myelodysplastic Syndromes

We believe there is a significant need for a safer, more effective, and more convenient option to address anemia in patients with lower-risk MDS. Roxadustat, our orally administered small molecule HIF-PH inhibitor, stimulates the body's natural mechanism of red blood cell production and iron hemostasis based on cellular-level oxygen-sensing and iron-regulation mechanisms. Unlike ESAs which are limited to providing exogenous EPO, roxadustat activates a coordinated erythropoietic response in the body that includes the stimulation of red blood cell progenitors, an increase in the body's production of endogenous EPO, and an increase in iron availability for hemoglobin synthesis, which we believe is important in a broad range of MDS patients. Moreover, in anemia of CKD, roxadustat has demonstrated the ability in clinical trials to increase and maintain hemoglobin levels in the presence of inflammation as measured by CRP, where ESAs have shown limited effect. We believe that roxadustat has the potential to replicate this result in MDS anemia patients, where it is not uncommon for patients to present with autoimmune and inflammatory conditions.

Clinical Development of Roxadustat in Myelodysplastic Syndromes

We are continuing to enroll MATTERHORN, our Phase 3 placebo controlled, double-blind clinical trial to evaluate the safety and efficacy of roxadustat for treatment of anemia in MDS in the U.S. and Europe. This 160-patient trial is studying roxadustat in transfusion-dependent, lower-risk MDS patients, in which subjects are randomized 3:2 to receive roxadustat or placebo three-times-weekly. The primary endpoint is the proportion of patients who achieve transfusion independence by 28 weeks with secondary endpoints and safety evaluated at 52 weeks. We expect topline data from this study in the first half of 2022.

In the open-label dose-finding component of this study, 24 lower-risk, transfusion dependent MDS patients with anemia were enrolled in three sequential starting dose cohorts (1.5 mg/kg, 2.0 mg/kg, and 2.5 mg/kg), with roxadustat doses adjusted every eight weeks per a pre-defined algorithm based on hemoglobin response. Best supporting care including red blood cell transfusion was allowed, as needed, per investigator's discretion. Patients treated with roxadustat achieved a greater than or equal to 8-week transfusion independence rate of 38% in the first 28 weeks and 54% of patients had greater than or equal to 50% reduction in red blood cell transfusion over any eight weeks, from baseline. Roxadustat was generally well tolerated in each dose cohort. The dose level of 2.5 mg/kg was selected as the starting dose for the double-blind component of the study.

In China, we are preparing to enroll the Phase 3 double-blind, placebo-controlled portion of our Phase 2/3 clinical trial to evaluate the safety and efficacy of roxadustat in non-transfusion dependent, lower-risk MDS patients with anemia. One hundred thirty-five subjects will be randomized 2:1 to receive roxadustat or placebo three-times weekly for 26 weeks. The primary endpoint for this study is percentage of patients achieving a hemoglobin response.

PAMREVLUMAB FOR THE TREATMENT OF FIBROSIS AND CANCER

We were founded to discover and develop therapeutics for fibrosis and began studying CTGF shortly after its discovery. Our accumulated discovery research efforts indicate that CTGF is a critical common element in the progression of serious diseases associated with fibrosis.

From our library of human monoclonal antibodies that bind to different parts of the CTGF protein and block various aspects of CTGF biological activity, we selected pamrevlumab, for which we have exclusive worldwide rights. We believe that pamrevlumab blocks CTGF and inhibits its central role in causing diseases associated with fibrosis. Our data to date indicate that pamrevlumab is a promising and highly differentiated product candidate with broad potential to treat a number of fibrotic diseases and cancers.

We are currently conducting Phase 3 studies in pancreatic cancer, IPF and DMD. In the U.S., the FDA has granted Orphan Drug Designation to pamrevlumab for the treatment of IPF, LAPC, and DMD. In addition, the EMA has granted Orphan Medicinal Product Designation to pamrevlumab for the treatment of DMD. Pamrevlumab has also received Fast Track designation from the FDA for the treatment of both IPF and LAPC.

Overview of Fibrosis

Fibrosis is an aberrant response of the body to tissue injury that may be caused by trauma, inflammation, infection, cell injury, or cancer. The normal response to injury involves the activation of cells that produce collagen and other components of the extracellular matrix ("ECM") that are part of the healing process. This healing process helps to fill in tissue voids created by the injury or damage, segregate infections or cancer, and provide strength to the recovering tissue. Under normal circumstances, where the cause of the tissue injury is limited, the scarring process is self-limited and the scar resolves to approximate normal tissue architecture. However, in certain disease states, this process is prolonged and excessive and results in progressive tissue scarring, or fibrosis, which can cause organ dysfunction and failure as well as, in the case of certain cancers, promote cancer progression.

Excess CTGF levels are associated with fibrosis. CTGF increases the abundance of myofibroblasts, a cell type that drives wound healing, and stimulates them to deposit ECM proteins such as collagen at the site of tissue injury. In the case of normal healing of a limited tissue injury, myofibroblasts eventually die by programmed cell death, or apoptosis, and the fibrous scarring process recedes.

Multiple biological agents and pathways have been implicated in the fibrotic process, many of which converge on CTGF, a central mediator of fibrosis. In the case of cancer, the sustained tumor-associated fibrotic tissue promotes tumor cell survival and metastasis. CTGF is a secreted glycoprotein produced by fibroblasts, endothelium, mesangial cells and other cell types, including cancers, and is induced by a variety of regulatory modulators, including TGF-\(\theta\) and VEGF. CTGF expression has been demonstrated to be up-regulated in fibrotic tissues. Thus, we believe that targeting CTGF to block or inhibit its activity could mitigate, stop or reverse tissue fibrosis. In addition, since CTGF is implicated in nearly all forms of fibrosis, we believe pamrevlumab has the potential to provide clinical benefit in a wide range of clinical indications that are characterized by fibrosis.

Until recently, it was believed that fibrosis was an irreversible process. It is now generally understood that the process is dynamic and potentially amenable to reversal. Based on studies in animal models of fibrosis of the liver, kidney, muscle and cardiovascular system, it has been shown that fibrosis can be reversed. It has also been demonstrated in humans that fibrosis caused by hepatitis virus can be reversed (Chang et al. Hepatology (2010)). Additionally, we have generated data in human and animal studies that lung fibrosis progression can be slowed, arrested, or possibly reversed in some instances upon treatment with pamrevlumab.

Clinical Development of Pamrevlumab - Overview

We have performed clinical trials of pamrevlumab in IPF, pancreatic cancer, liver fibrosis and diabetic kidney disease. In eleven Phase 1 and Phase 2 clinical studies involving pamrevlumab to date, including more than 600 patients who were treated with pamrevlumab (about half of patients dosed for more than six months), pamrevlumab has been well-tolerated across the range of doses studied, and there have been no dose-limiting toxicities seen thus far.

Idiopathic Pulmonary Fibrosis

Understanding IPF and Current Therapies

IPF is a form of progressive pulmonary fibrosis, or abnormal scarring, which destroys the structure and function of the lungs. As tissue scarring progresses in the lungs, transfer of oxygen into the bloodstream is increasingly impaired. Average life expectancy at the time of confirmed diagnosis of IPF is estimated to be between three to five years, with approximately two-thirds of patients dying within five years of diagnosis. Thus, the survival rates are comparable to some of the most deadly cancers. The cause of IPF is unknown but is believed to be related to unregulated cycles of injury, inflammation and fibrosis.

Patients with IPF experience debilitating symptoms, including shortness of breath and difficulty performing routine functions, such as walking and talking. Other symptoms include chronic dry, hacking cough, fatigue, weakness, discomfort in the chest, loss of appetite, and weight loss. Over the last decade, refinements in diagnosis criteria and enhancements in high-resolution computed tomography imaging technology ("quantitative HRCT") have enabled more reliable diagnosis of IPF without the need for a lung biopsy.

The U.S. prevalence and incidence of IPF are estimated to be 44,000 to 135,000 cases, and 21,000 new cases per year, respectively, based on Raghu et al. (Am J Respir Crit Care Med (2006)) and on data from the United Nations Population Division. We believe that with the availability of technology to enable more accurate diagnoses, the number of individuals diagnosed per year with IPF will continue to increase.

There are currently two therapies approved to treat IPF in Europe and the U.S., pirfenidone and nintedanib. The approvals and subsequent launches of Esbriet (pirfenidone) and Ofev (nintedanib) have clearly shown the commercial potential in IPF. Hoffmann-La Roche ("Roche") reported worldwide sales of approximately \$1.1 billion for 2019 and \$1.2 billion for 2020 for Esbriet® (pirfenidone). Similarly, Boehringer Ingelheim Pharma GmbH & Co. KG ("Boehringer Ingelheim") reported total sales of approximately \$1.3 billion for Ofev® (nintedanib) in 2018, and approximately \$1.7 billion in 2019.

Phase 3 Clinical Development - Randomized, Double-Blind, Placebo-Controlled Trials of Pamrevlumab in IPF

We are conducting ZEPHYRUS-1, our Phase 3 trial of pamrevlumab in IPF patients, as well as our newly initiated ZEPHYRUS-2, a second IPF Phase 3 study. Both studies are double-blind, placebo-controlled Phase 3 trials targeting approximately 340 patients, each with a primary U.S. efficacy endpoint of change from baseline in forced vital capacity.

The primary efficacy endpoint in Europe for each study is disease progression (defined by a decline in forced vital capacity ("FVC") percent predicted of greater than or equal to 10% or death). Secondary endpoints will include clinical outcomes of disease progression, patient reported outcomes, and quantitative changes in lung fibrosis volume from baseline.

The COVID-19 pandemic has affected enrollment in these IPF trials, more so than our other studies due to the vulnerability of this patient population. In addition to efforts we are making in ensuring patient safety, we are also working to expand enrollment through a number of methods, including expanding the number of clinical sites in China.

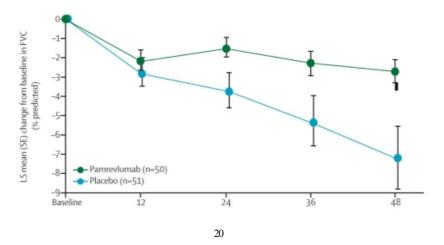
PRAISE - Study 067 - Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial of Pamrevlumab in IPF

In September 2019, positive results from PRAISE, our randomized, double-blind, placebo-controlled Phase 2 clinical trial (Study 067), were published in *The Lancet Respiratory Medicine*. PRAISE was designed to evaluate the safety and efficacy of pamrevlumab in patients with mild-to-moderate IPF (baseline FVC percentage predicted of 55%), as well as topline results from two sub-studies that were added to evaluate the safety of combining pamrevlumab with approved IPF therapies.

In the double-blind, placebo-controlled 48-week portion of this study, 103 patients were randomized (1:1) to receive either 30mg/kg of pamrevlumab or placebo intravenously every three weeks. Lung function assessments were conducted at baseline and at Weeks 12, 24, 36 and 48. Quantitative HRCT assessments were performed at baseline and at Weeks 24 and 48.

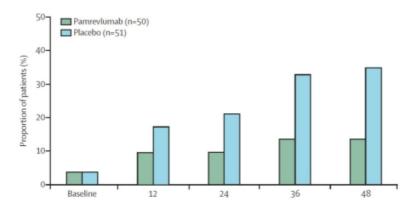
Pamrevlumab met the primary efficacy endpoint of change of FVC percent predicted, a measure of a patient's lung volume as a percentage of what would be expected for such patient's age, race, sex and height. The average decline (least squares mean) in FVC percent predicted from baseline to Week 48 was 2.9 in the pamrevlumab arm (n=50) as compared to an average decline of 7.2 in the placebo arm (n=51), a statistically significant difference of 4.33 (p=0.033).

FVC Change by Visit



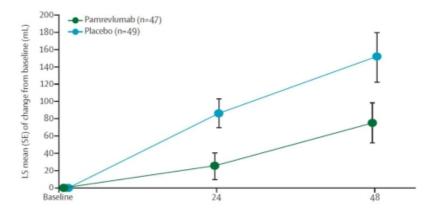
Pamrevlumab-treated patients had an average decrease (least squares mean) in FVC of 129 ml at Week 48 compared to an average decrease of 308 ml in patients receiving placebo, a statistically significant difference of 178 ml (p=0.0249, using a linear slope analysis in the intent-to-treat population). This represents a 57.9% relative difference. In addition, the pamrevlumab-treated arm had a lower proportion of patients (10%) who experienced disease progression (defined by a decline in FVC percent predicted of greater than or equal to 10% or death), than did the placebo arm (31.4%) at Week 48 (p=0.0103).

Proportion of Patients with Decline in Percentage of Predicted FVC of 10% or Greater, or Death, by Visit



In this study, we measured change in quantitative lung fibrosis ("QLF") from baseline to Week 24 and Week 48 using quantitative HRCT. The pamrevlumab arm achieved a statistically significant reduction in the rate of progression of lung fibrosis compared to placebo using HRCT to measure QLF. The change in QLF volume from baseline to Week 24 for pamrevlumab-treated patients was 24.8 ml vs. 86.4 ml for placebo, with a treatment difference of -61.6 ml, p=0.009. The change in QLF volume from baseline to 48 weeks was 75.4 ml in pamrevlumab-treated patients vs. 151.5 ml in patients on placebo, with a treatment difference of -76.2 ml, p=0.038.

Change from Baseline in Volume of Quantitative Lung Fibrosis (mL) in the Intention-to-Treat Population



As in our previous open label Phase 2 study, a correlation between FVC percent predicted and QLF was confirmed at both Week 24 and 48 in this study.

We are not aware of any other IPF therapies that have shown a statistically significant effect on lung fibrosis as measured by quantitative HRCT analysis.

The treatment effects of pamrevlumab were demonstrated not only on change in FVC, a measure of pulmonary function and IPF disease progression, and change in fibrosis using quantitative HRCT, but pamrevlumab-treated patients also showed a trend of clinically meaningful improvement in a measure of health-related quality of life using the St. George's Respiratory Questionnaire (SGRQ) vs. a reduction in quality of life seen in placebo patients over the 48 weeks of treatment. The SGRQ quality of life measurement has been validated in chronic obstructive pulmonary disease. In the patients that were evaluated by the UCSD Shortness of Breath Questionnaire, pamrevlumab-treated patients had a significant attenuation of their worsening dyspnea in comparison to placebo patients.

Pamrevlumab was well-tolerated in the placebo-controlled study. The treatment-emergent adverse events were comparable between the pamrevlumab and placebo arms and the adverse events in the pamrevlumab arm were consistent with the known safety profile of pamrevlumab. In this study, as compared with the placebo group, fewer pamrevlumab patients were hospitalized, following an IPF-related or respiratory treatment-emergent adverse event, or died for any reason.

The double-blind, active-controlled combination sub-studies were designed to assess the safety of combining pamrevlumab with standard of care medication in IPF patients. Study subjects were on stable doses of pirfenidone or nintedanib for at least three months and were randomized 2:1 to receive 30 mg/kg of pamrevlumab or placebo every three weeks for 24 weeks. Thirty-six patients were enrolled in the pirfenidone sub-study and 21 patients were enrolled in the nintedanib sub-study. Pamrevlumab appeared to be well-tolerated when given in combination with either pirfenidone or nintedanib.

Study 049 - Open-Label Phase 2 Trial of Pamrevlumab in IPF

Our completed open-label extension of Study 049, a Phase 2 open-label, dose-escalation study to evaluate the safety, tolerability, and efficacy of pamrevlumab in 89 patients with IPF, was consistent with our results from our randomized, double-blind, placebo-controlled Phase 2 clinical trial PRAISE. We presented data from our open-label Phase 2 IPF extension study (049) at the International Colloquium on Lung and Airway Fibrosis in November 2016, reporting that no safety issues were observed during prolonged treatment with pamrevlumab. Some of the 37 patients who enrolled in the extension study were treated with pamrevlumab for up to five years. Trends regarding improved or stable pulmonary function and stable fibrosis observed during the initial one-year study were also observed in the extension study.

Pancreatic Cancer

Understanding Pancreatic Cancer and the Limitations of Current Therapies

Certain solid malignant tumors have a prominent fibrosis component consisting mostly of ECM that contributes to metastasis and progressive disease. ECM is the connective tissue framework of an organ or tissue.

Pancreatic ductal adenocarcinoma, or pancreatic cancer, is the third leading cause of cancer deaths in the U.S. According to the European Commission's European Cancer Information System, there were 100,005 new cases of pancreatic cancer and 95,373 deaths from pancreatic cancer in Europe projected for 2018. The National Cancer Center of Japan estimated that there were 36,239 new cases of pancreatic cancer in 2014, increased from 24,442 cases in 2004. In its report of December 2017, Decision Resources Group estimated that the major market sales (U.S., Europe and Japan) of pancreatic cancer drugs will grow from \$1.3 billion in 2016 to approximately \$3.7 billion in 2026. According to the U.S. National Cancer Institute, there were an estimated 57,000 new cases of pancreatic cancer in the U.S. in 2019. Fifty percent of new cases are metastatic. Another 15-20% have localized resectable tumors. The remaining 30-35% have localized but unresectable tumors.

For those with non-resectable tumors, median survival is eight to 12 months post-diagnosis, and about 8% realize five years of survival; similar to metastatic cases. For those with resectable tumors, 50% survive 17 to 27 months post-diagnosis and ~20% report five-year survival.

Pancreatic cancer is aggressive and typically not diagnosed until it is largely incurable. Most patients are diagnosed after the age of 45, and according to the American Cancer Society, 94% of patients die within five years from diagnosis. The majority of patients are treated with chemotherapy, but pancreatic cancer is highly resistant to chemotherapy. Approximately 15% to 20% of patients are treated with surgery; however, even for those with successful surgical resection, the median survival is approximately two years, with a five-year survival rate of 15% to 20% (Neesse et al. Gut (2011)). Radiation treatment may be used for locally advanced diseases, but it is not curative.

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The duration of effect of approved anti-cancer agents to treat pancreatic cancer is limited. Gemcitabine demonstrated improvement in median overall survival from approximately four to six months, and erlotinib in combination with gemcitabine demonstrated an additional ten days of survival. Nab-paclitaxel in combination with gemcitabine was approved by the FDA in 2013 for the treatment of pancreatic cancer, having demonstrated median survival of 8.5 months. The combination of folinic acid, 5-fluorouracil, irinotecan and oxaliplatin (FOLFIRINOX) was reported to increase survival to 11.1 months from 6.8 months with gemcitabine. These drugs illustrate that progress in treatment for pancreatic cancer has been modest, and there remains a need for substantial improvement in patient survival and quality of life.

The approved chemotherapeutic treatments for pancreatic cancer target the cancer cells themselves. Tumors are composed of cancer cells and associated non-cancer tissue, or stroma, of which ECM is a major component. In certain cancers such as pancreatic cancer, both the stroma and tumor cells produce CTGF which in turn promotes the proliferation and survival of stromal and tumor cells. CTGF also induces ECM deposition that provides advantageous conditions for tumor cell adherence and proliferation, promotes blood vessel formation, or angiogenesis, and promotes metastasis, or tumor cell migration, to other parts of the body.

Pancreatic cancers are generally resistant to powerful chemotherapeutic agents, and there is now growing interest in the use of an anti-fibrotic agent to diminish the supportive role of stroma in tumor cell growth and metastasis. The anti-tumor effects observed with pamrevlumab in preclinical models indicate that it has the potential to inhibit tumor expansion through effects on tumor cell proliferation and apoptosis as well as reduce metastasis.

Phase 3 Clinical Development - Randomized, Double-Blind, Placebo-Controlled Trial of Pamrevlumab in Locally Advanced, Unresectable Pancreatic Cancer

We continue to enroll LAPIS, our double-blind placebo controlled Phase 3 clinical program for pamrevlumab as a neoadjuvant therapy for LAPC. We intend to enroll approximately 260 patients, randomized at a 1:1 ratio to receive either pamrevlumab or placebo, in each case in combination with gemcitabine and nab-paclitaxel. We expect topline resection data from this study in the second half of 2022.

Study 069 - Randomized, Open-Label, Active-Controlled Phase 1/2 Trial of Pamrevlumab in Locally Advanced Pancreatic Cancer

We continue to follow patients in our ongoing open-label, randomized (2:1) Phase 1/2 trial (FGC004C-3019-069) of pamrevlumab combined with gemcitabine plus nab-paclitaxel chemotherapy vs. the chemotherapy regimen alone in patients with inoperable locally advanced pancreatic cancer that has not been previously treated. We enrolled 37 patients in this study and completed the six-month treatment period and surgical assessment at the end of 2017. The overall goal of the trial is to determine whether the pamrevlumab combination can convert inoperable pancreatic cancer to operable, or resectable, cancer. Tumor removal is the only chance for cure of pancreatic cancer, but only approximately 15% to 20% of patients are eligible for surgery.

We reported updated results from this ongoing study at the American Society of Clinical Oncology Annual Meeting in June 2018. A higher proportion (70.8%) of pamrevlumab-treated patients whose tumors were previously considered unresectable became eligible for surgical exploration than patients who received chemotherapy alone (15.4%), based on pre-specified eligibility criteria at the end of 6 months of treatment. Furthermore, a higher proportion of pamrevlumab-treated patients (33.3%) achieved surgical resection than those who received chemotherapy alone (7.7%).

In addition, this data showed improved overall survival among patients whose tumors were resected vs. not resected (NE vs. 18.56 months, p-value=0.0141) and a trend toward improved overall survival in patients eligible for surgery vs. patients who were not (27.73 vs. 18.40 months, p-value=0.0766). All of the patients on study at the time of the results reported in June 2018 continue to remain on study. No increase in serious adverse events was observed in the pamrevlumab arm and no delay in wound healing was observed post-surgery.

Patients with LAPC have median survival of less than 12 months, only slightly better than patients with metastatic pancreatic cancer, whereas patients with resectable pancreatic cancer have a much better prognosis with median survival of approximately 23 months and some patients being cured. If pamrevlumab in combination with chemotherapy continues to demonstrate an enhanced rate of conversion from unresectable cancer to resectable cancer, it may support the possibility that pamrevlumab could provide a substantial survival benefit for locally advanced pancreatic cancer patients.

Completed Clinical Trials of Pamrevlumab in Pancreatic Cancer

We completed an open-label Phase 1/2 (FGCL-MC3019-028) dose finding trial of pamrevlumab combined with gemcitabine plus erlotinib in patients with previously untreated locally advanced (Stage 3) or metastatic (Stage 4) pancreatic cancer. These study results were published in the *Journal of Cancer Clinical Trials* (Picozzi et al., J Cancer Clin Trials 2017, 2:123). Treatment continued until progression of the cancer or the patient withdrew for other reasons. Patients were then followed until death.

Seventy-five patients were enrolled in this study with 66 (88%) having Stage 4 metastatic cancer. The study demonstrated a dose-related increase in survival. At the lowest doses, no patients survived for even one year while at the highest doses up to 31% of patients survived one year.

A post-hoc analysis found that there was a significant relationship between survival and trough levels of plasma pamrevlumab measured immediately before the second dose (Cmin), as illustrated below. Cmin greater than or equal to $150~\mu g/mL$ was associated with significantly improved progression-free survival (p=0.01) and overall survival (p=0.03) vs. those patients with Cmin less than $150~\mu g/mL$. For patients with Cmin >150 $\mu g/mL$ median survival was 9.0 months compared to median survival of 4.4 months for patients with Cmin <150 $\mu g/mL$. Similarly, 34.2% of patients with Cmin >150 $\mu g/mL$ survived for longer than one year compared to 10.8% for patients with Cmin <150 $\mu g/mL$. These data suggest that sufficient blockade of CTGF requires pamrevlumab threshold blood levels of approximately $150~\mu g/mL$ in order to improve survival in patients with advanced pancreatic cancer.

Increased Pancreatic Cancer Survival Associated with Increased Plasma Levels of Pamrevlumab

The Kaplan-Meier plot provides a representation of survival of all patients in the clinical trial. Each vertical drop in the curve represents a recorded event (death) of one or more patients. When a patient's event cannot be determined either because he or she has withdrawn from the study or because the analysis is completed before the event has occurred, that patient is "censored" and denoted by a symbol (•) on the curve at the time of the last reliable assessment of that patient.

Overall Survival Time (Months)

In the study, the majority of adverse events were mild to moderate, and were consistent with those observed for erlotinib plus gemcitabine treatment without pamrevlumab. There were 99 treatment-emergent serious adverse events; six of which were assessed as possibly related to the investigational drug by the principal investigator, and 93 as not related to study treatment. After investigation, it is our belief that there is no causal relationship between pamrevlumab and the treatment-emergent serious adverse events deemed possibly related by the principal investigator. We did not identify any evolving dose-dependent pattern, and higher doses of pamrevlumab were not associated with higher numbers of serious adverse events or greater severity of the serious adverse events observed.

Pamrevlumab for Duchenne Muscular Dystrophy

Understanding DMD and the Limitations of Current Therapies

In the U.S., approximately one in every 5,000 boys have DMD, and approximately 20,000 children are diagnosed with DMD globally each year. There are currently no approved disease-modifying treatments. Despite taking steroids to mitigate progressive muscle loss, a majority of children with DMD are non-ambulatory by adolescence and median survival is age 25.

DMD is an inherited disorder of one of the dystrophin genes resulting in absence of the dystrophin protein and abnormal muscle structure and function, leading to progressively diminished mobility as well as pulmonary function and cardiac function, which result in early death. Constant myofiber breakdown results in persistent activation of myofibroblasts and altered production of ECM resulting in extensive fibrosis in skeletal muscles of DMD patients. Desguerre et al. (2009) showed that muscle fibrosis was the only myo-pathologic parameter that significantly correlated with poor motor outcome as assessed by quadriceps muscle strength, manual muscle testing of upper and lower limbs, and age at ambulation loss. Numerous pre-clinical studies including those in the mdx model of DMD suggest that CTGF contributes to the process by which muscle is replaced by fibrosis and fat and that CTGF may also impair muscle cell differentiation during muscle repair after injury.

Phase 3 Clinical Development - LELANTOS, a double-blind, placebo-controlled trial in non-ambulatory DMD patients

In the third quarter of 2020, we initiated a Phase 3 clinical trial, LELANTOS 1, evaluating pamrevlumab as a treatment for DMD. LELANTOS 1 is a double-blind, placebo-controlled trial in approximately 90 non-ambulatory DMD patients. Patients will be randomized at a 1:1 ratio to pamrevlumab or placebo and have a treatment period of 52 weeks. The primary endpoint will assess change in upper limb strength and additional endpoints will include pulmonary, performance, cardiac, and fibrosis assessments.

We also plan to initiate a Phase 3 clinical trial, LELANTOS 2, evaluating pamrevlumab in 70 ambulatory DMD patients.

We expect topline data from these studies in the second half of 2022.

Phase 2 Open-Label Trial of Pamrevlumab in DMD

In June 2019 at the Parent Project Muscular Dystrophy meeting, we reported topline results from this 21 patient open-label single-arm trial in non-ambulatory DMD patients. This one-year administrative analysis compared our Phase 2 data to previously published natural disease history studies of DMD patients. While we cannot make direct comparisons between our trial and previously published data due to, among other things, differences in subject numbers, baseline characteristics, inclusion/exclusion criteria, treatment protocols, and analysis methods, we are encouraged by the data obtained so far. Pamrevlumab was well tolerated in this study.

In pulmonary function tests, the results from our study indicate a potential reduction in the 1-year decline in FVC percent predicted from baseline for pamrevlumab-treated patients when compared to FVC data of DMD patients (whether such patients were taking steroids or not) published in 2019 by Ricotti. In the 2019 Ricotti study, the DMD patients were treated with steroids only. Similarly, all of the patients in our Phase 2 pamrevlumab trial were on steroids. In addition, pamrevlumab showed less decline in both percent predicted forced expiratory volume as compared to previously published study results of Meier in 2016, and in percent predicted peak expiratory flow rate, compared to what was observed in the study by Ricotti in 2019

Our data showed an increase in cardiac function, measured by mean change of left ventricular ejection fraction ("LVEF"), of 0.29% from baseline for pamrevlumab-treated patients. Whereas, data published in 2018 by McDonald of DMD patients only on steroids showed a mean LVEF decline of 0.82% from baseline in one year.

In muscle function tests, the majority of the results of this Phase 2 study showed the mean change from baseline in pamrevlumab-treated patients were more favorable than previously published data. Our results showed a positive increase in grip-strength score in both dominant and non-dominant hands at one year of treatment with pamrevlumab, while earlier results from a 2015 study by Seferian showed a decline at one year as expected. In the performance of the upper limb ("PUL") test specifically developed for DMD patients, pamrevlumab-treated patients had a mean change from baseline of -1.53. In the 2019 study by Ricotti of DMD patients taking either nothing or only steroids, the annual mean change in the PUL test was -4.13. Furthermore, in our study a strong correlation between change in biceps brachii T2-mapping and change in PUL score was observed, demonstrating stabilization and even possible improvement in the muscle fibrosis burden.

Commercialization Strategy for Pamrevlumab

Our goal, if pamrevlumab is successful, is to be a leader in the development and commercialization of novel approaches for inhibiting fibrosis and treating certain forms of cancer and muscular dystrophy diseases. To date, we have retained exclusive worldwide rights for pamrevlumab. We have commenced brand development activities for pamrevlumab and will be advancing these efforts in preparation for potential launches in IPF, LAPC and DMD, consistent with the approaches of companies with a product in late-stage clinical development.

Research at FibroGen

Our research programs at FibroGen are grounded in our three areas of expertise: HIF biology, 2-oxoglutarate enzymology, and CTGF biology.

We have applied our expertise in the field of HIF-PH inhibition to develop an understanding of other areas of HIF biology with important therapeutic implications. This consistent progression of discovery has led to findings relating to HIF-mediated effects associated with inflammatory pathways, various aspects of iron metabolism, insulin sensitivity and glucose and fat metabolism, neurological disease, and ischemic injury. There are at least three different HIF-PH enzymes that are known to regulate the stability of HIF - these enzymes are commonly referred to in the scientific literature as PHD1, PHD2 and PHD3. Studies of genetically modified mice, in which the individual HIF-PH enzymes have been deleted, have revealed that PHD2 plays a major role in the regulation of erythropoiesis by HIF. In contrast, PHD1 and PHD3 appear to play less important roles in HIF-mediated erythropoiesis, but instead have been implicated in other important biological pathways. We believe that both pan-PHD and PHD-selective inhibitors could have important therapeutic applications beyond anemia.

The HIF-PH enzymes that are the targets of roxadustat belong to a broader family of enzymes known as 2-oxoglutarate (2OG)-dependent oxygenases. In humans, this family comprises more than 60 members that play important roles in a diverse range of biological processes including collagen biosynthesis, oxygen sensing, epigenetic regulation, nucleic acid modification/repair, and lipid metabolism. The first members of this enzyme family to be characterized were the collagen prolyl hydroxylases, which play a critical role in the biosynthesis of collagen and as a result, are potential targets for the treatment of fibrotic disease. Other members of the 2OG-dependent oxygenase family with relevance to human disease include the Jumonji domain-containing histone demethylases, which are emerging cancer targets.

The fact that all members of the 2OG-dependent oxygenase enzyme family use 2OG as a co-substrate makes them viable targets for small molecule inhibitors that compete with 2OG. FibroGen has been a leader in inhibition of enzymes belonging to this family, and our internal medicinal chemistry efforts have generated a library of novel compounds designed to target the 2OG-dependent oxygenase family.

Finally, we have applied our knowledge of CTGF to investigate additional applications of agents that interfere with the role of this protein in disease. In some instances, we are exploring direct engagement of CTGF itself. In other instances, we are studying the regulation of CTGF.

COLLABORATIONS

Our revenue to date has been generated primarily from our collaboration agreements with Astellas and AstraZeneca for the development and commercialization of roxadustat. In addition, we started roxadustat commercial sales in China in the third quarter of 2019. For fiscal year ended December 31, 2020, 58% of our revenue was related to our collaboration agreements, and 42% of our revenue was from roxadustat commercial sales in China. For the fiscal years ended December 31, 2019 and 2018, substantially all of our revenue was related to our collaboration agreements.

Astellas

We have two agreements with Astellas for the development and commercialization of roxadustat, one for Japan, and one for Europe, the Commonwealth of Independent States, the Middle East and South Africa. Under these agreements, we provided Astellas the right to develop and commercialize roxadustat for anemia in these territories.

We share responsibility with Astellas for clinical development activities required for U.S. and Europe regulatory approval of roxadustat, and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will hold and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements, other than roxadustat drug product for Japan. Astellas is responsible for roxadustat commercialization activities in the Astellas territories.

AstraZeneca

We also have two agreements with AstraZeneca for the development and commercialization of roxadustat for anemia, one for China (the "China Agreement"), and one for the U.S. and all other countries not previously licensed to Astellas (the "U.S./RoW Agreement"). Under these agreements, we provided AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories. We share responsibility with AstraZeneca for clinical development activities required for U.S. regulatory approval of roxadustat, and FibroGen will transfer the U.S. NDA to AstraZeneca upon approval. AstraZeneca will hold the equivalent regulatory filings in the other licensed countries.

In China, our subsidiary FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") has conducted the development work for CKD anemia and will continue to hold all of the regulatory licenses issued by China regulatory authorities and be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is also responsible for 100% of development expenses in all other licensed territories outside of China. We are responsible, ourselves and through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the AstraZeneca agreements.

Under the China Agreement, which is conducted through FibroGen China Anemia Holdings, Ltd. ("FibroGen Cayman"), FibroGen Beijing, and FibroGen International (Hong Kong) Limited (collectively, "FibroGen China"), the commercial collaboration is structured as a 50/50 profit share, which was restructured in the third quarter of 2020. Pursuant to an Amendment to the China Agreement, the parties agreed to establish a jointly owned entity to conduct distribution. FibroGen Beijing will manufacture and transfer commercial product to the distribution entity in exchange for a transfer price at a percentage of net sales. AstraZeneca will conduct sales and marketing activities in China for roxadustat, which will be billed to the distribution entity, subject to a cap of a percentage of roxadustat net sales until AstraZeneca has recouped its sales and marketing expenses, at which time it will bill actual expenses, subject to the cap.

Additional Information Related to Collaboration Agreements

Additional information related to our collaboration agreements is set forth in Item 7 of this Annual Report on Form 10-K, and Note 4, *Collaboration Agreements and Revenues*, to our consolidated financial statements under Item 8 of this Annual Report. Information about collaboration partners that accounted for more than 10% of our total revenue or accounts receivable for the last three fiscal years is set forth in Note 15, *Segment and Geographic Information*, to our consolidated financial statements under Item 8 of this Annual Report.

COMPETITION

The pharmaceutical and biotechnology industries are highly competitive, particularly in some of the indications we are developing drug candidates, including anemia in CKD, IPF, pancreatic cancer, and DMD. We face competition from multiple other pharmaceutical and biotechnology companies, many of which have significantly greater financial, technical and human resources and experience in product development, manufacturing and marketing. These potential advantages of our competitors are particularly a risk in IPF, pancreatic cancer, and DMD, where we do not currently have a development or commercialization partner.

We expect any products that we develop and commercialize to compete based on, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition, and the availability of reimbursement from government and other third-party payors.

When any of our product candidates are approved, they will compete with currently marketed products, and product candidates that may be approved for marketing in the future, for treatment of the indications described below.

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In addition, we will likely face competition from other companies developing treatments of other anemia indications that we may also seek to pursue in the future or that may be sold in indications we are pursuing but for which they are not yet approved. We may face competition for patient recruitment, enrollment for clinical trials, and potentially in commercial sales. There may also be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat.

Roxadustat

Approved Medicines

Drugs that will compete with roxadustat are expected to include ESAs, particularly in those patient segments where ESAs are used. Some of the available ESAs include epoetin alfa (EPOGEN® marketed by Amgen Inc. in the U.S., Procrit® and Erypo®/Eprex®, marketed by Johnson & Johnson, Inc. and Espo® marketed by Kyowa Hakko Kirin in Japan and China), darbepoetin (Amgen/Kyowa Hakko Kirin's Aranesp® and NESP®) and Mircera® marketed by Roche outside the U.S. and by Vifor Pharma, a Roche licensee, in the U.S. and Puerto Rico, as well as biosimilar versions of these currently marketed ESA products. ESAs have been used in the treatment of anemia in CKD for more than 30 years, serving a significant majority of dialysis patients. While non-dialysis CKD anemia patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated, some patients under nephrology or hematology care may be receiving ESA therapy. It may be difficult to encourage healthcare providers and patients to switch to roxadustat from products with which they have become familiar.

Biosimilars

The first biosimilar ESA, Pfizer's Retacrit® (epoetin zeta), entered the U.S. market in November 2018. Market penetration of Retacrit and the potential addition of other biosimilar ESAs currently under development may alter the competitive and pricing landscape of anemia therapy in CKD patients on dialysis under the end-stage renal disease bundle. The patients for Amgen's EPOGEN® (epoetin alfa) expired in 2004 in Europe, and the final material patients in the U.S. expired in May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in Europe, China and other territories. In the U.S., a few ESA biosimilars are currently under development. Sandoz, a division of Novartis, markets Binocrit® (epoetin alfa) in Europe and may file a biosimilar Biologics License Application in the U.S.

Product Candidates in Development

We may also face competition from potential new anemia therapies currently in clinical development, including in those patient segments not adequately addressed by ESAs. Companies that are currently developing HIF-PH inhibitors for anemia in CKD indications include GlaxoSmithKline plc ("GSK"), Bayer Corporation ("Bayer"), Akebia Therapeutics, Inc. ("Akebia"), Otsuka Pharmaceutical ("Otsuka"), Akebia's partner in the U.S. and Europe, Japan Tobacco, and Zydus Cadila (India) ("Zydus"). Akebia has completed Phase 3 studies in CKD patients on dialysis and not on dialysis in the U.S., as well as a Phase 3b, randomized, open-label, active-controlled trial evaluating the efficacy and safety of oral vadadustat once daily and three times weekly for the maintenance treatment of anemia in hemodialysis subjects converting from erythropoiesis stimulating agents. The study completion date is estimated to be May 2022. Akebia announced an additional Phase 3 study evaluating the efficacy and safety of dose conversion from a long-acting erythropoiesis stimulating agent (Mircera®) to three times weekly oral vadadustat for the maintenance treatment of anemia in hemodialysis subjects. The estimated study start date is February 2021. Akebia has publicly stated their intent to file the vadadustat NDA in the U.S. in the second quarter of 2021.

Japan

In Japan, Mitsubishi Tanabe Pharmaceutical Corporation, Akebia's collaboration partner, received approval for vadadustat on June 29, 2020 for the treatment of anemia of CKD patients on and not on dialysis. GSK received approval for daprodustat in Japan on June 29, 2020 for the treatment of anemia of CKD patients on and not on dialysis. Price listing for the launch in Japan of both vadadustat and daprodustat occurred in the third quarter of 2020, with pricing in line with roxadustat pricing. GSK is also conducting global Phase 3 studies in CKD patients on dialysis and not on dialysis, and expects to complete those studies by March 2022. GSK and Kyowa Hakko Kirin announced in November 2018 that the two companies signed a strategic commercialization deal in Japan for daprodustat. Bayer has completed global Phase 2 studies and its HIF-PH inhibitor is now in Phase 3 development in CKD populations on dialysis and not on dialysis in Japan. Japan Tobacco received approval in Japan for enarodustat for the treatment of anemia in CKD patients on dialysis and not on dialysis, to be sold by Torii Pharmaceuticals Ltd as ENAROY®. Japan Tobacco and its partner JW Pharmaceuticals started a Phase 3 study in dialysis patients in Korea in 2019. Zydus started Phase 3 studies in dialysis and non-dialysis CKD patients in India in 2019.

China

In China, biosimilars of epoetin alfa are offered by Chinese pharmaceutical companies such as EPIAO marketed by 3SBio Inc. as well as more than 15 other local manufacturers. We may also face competition by HIF-PH inhibitors from other companies such as Akebia, Bayer, and GSK, which was authorized by the National Medical Products Administration ("NMPA") to conduct trials in China to support its ex-China regulatory filings. Two domestic companies, Jiangsu Hengrui Medicine Co., Ltd. and Guandong Sunshine Health Investment Co., Ltd, have been permitted by the NMPA to conduct clinical trials for CKD anemia patients both on dialysis and not on dialysis, and 3SBio Inc. has submitted a clinical trial application to the NMPA to initiate trials for their HIF-PH inhibitor. Another domestic company, China Medical System Holdings Ltd., in-licensed desidustat, a compound that is currently in Phase 3 trials in India, from Zydus for greater China in January 2020. In January 2021, China Medical System Holdings Ltd. was granted approval by the NMPA in China to begin trials for desidustat in patients with anemia of CKD, including dialysis and non-dialysis patients. Shenzhen Salubris Pharmaceutical Co., Ltd., a domestic company in China, has in-licensed enarodustat from Japan Tobacco and received NMPA approval in the third quarter of 2020 to initiate Phase 3 studies. Akebia announced in April 2017 an expansion of their U.S. collaboration with Otsuka to add markets, including China. 3SBio Inc. announced in 2016 its plan to begin a Phase 1 clinical trial of a HIF-PH inhibitor for the China market.

CIA and MDS

In July 2020, Zydus received approval from the FDA to begin a Phase 1 study of desidustat for the treatment of CIA, which could potentially be competitive with roxadustat within this indication.

Reblozyl® (luspatercept) was approved by the FDA in April 2020 for the treatment of anemia in adults with MDS with ring sideroblasts or myelodysplastic/myeloproliferative neoplasms with ring sideroblasts and thrombocytosis who need regular red blood cell transfusions and have not responded well to or cannot receive an ESA. It is the first and only erythroid maturation agent approved in the U.S., Europe, and Canada and is part of a global collaboration between Acceleron Pharma, Inc. and Bristol Myers Squibb. In 2020, Reblozyl net revenue was \$274 million, including \$115 million in O4 2020.

Large Dialysis Organizations

The majority of the current CKD anemia market focuses on dialysis patients, who visit dialysis centers on a regular basis, typically three times a week, and anemia therapies are administered as part of the visit. Two of the largest operators of dialysis clinics in the U.S., DaVita Healthcare Partners Inc. ("DaVita"), and Fresenius Medical Care AG & Co. KGaA ("Fresenius"), collectively provide dialysis care to more than 80% of U.S. dialysis patients, and therefore have historically secured long-term contracts including rebate terms with Amgen. DaVita has a six-year sourcing and supply agreement with Amgen effective through 2022. Fresenius' contract with Amgen expired in 2015, following which Fresenius is providing Roche's ESA Mircera® to a significant portion of its U.S. dialysis patients. Successful penetration in this market may require our partner AstraZeneca to enter into an agreement with Fresenius, DaVita, or other dialysis organizations, on favorable pricing terms to each party.

Pamrevlumab

We are currently in Phase 3 development of pamrevlumab in IPF, locally advanced pancreatic cancer, and DMD. Most of our competitors have significantly more resources and expertise in development, commercialization and manufacturing, particularly due to the fact that we have not yet established a partnership for pamrevlumab. For example, both Roche and Boehringer Ingelheim, which market products for the treatment of IPF in the U.S., have successfully developed and commercialized drugs in various indications and have built sales organizations that we do not currently have; both have more resources and more established relationships when competing with us for patient recruitment and enrollment for clinical trials or, if we are approved, in the market.

Idiopathic Pulmonary Fibrosis

If approved and launched commercially to treat IPF, pamrevlumab is expected to compete with Roche's Esbriet® (pirfenidone), and Boehringer Ingelheim's Ofev® (nintedanib). We believe that if pamrevlumab can be shown to safely stabilize or reverse lung fibrosis, and thus stabilize or improve lung function in IPF patients, it can compete with pirfenidone and nintedanib for market share in IPF. However, it may be difficult to encourage treatment providers and patients to switch to pamrevlumab from a product with which they are already familiar. We may also face competition from potential new IPF therapies in recruitment and enrollment in our clinical trials and potentially in commercialization.

Pamrevlumab is administered via infusion, which may be more expensive and less convenient than small molecules such as nintedanib and pirfenidone. Other potential competitive product candidates in various stages of development for IPF include Kadmon Holdings, Inc.'s KD025, Liminal BioSciences' PBI-4050, and Roche/Promedior, Inc.'s PRM-151.

Pancreatic Cancer

We are developing pamrevlumab to be used in combination with Abraxane® (nab-paclitaxel) and gemcitabine in pancreatic cancer. Celgene's Abraxane was launched in the U.S. and Europe in 2013 and 2014, respectively, and was the first drug approved in this disease in nearly a decade. In 2015, Merrimack Pharmaceuticals Inc. ("Merrimack") received FDA approval for the use of ONIVYDE (irinotecan liposome injection, now licensed to Ipsen) for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy, and the combination therapy with Abraxane and gemcitabine became the first-line standard of care in these patients. As treatments for pancreatic cancer have shown limited success to date, combination therapies are expected, but the incremental cost may slow a new product adoption in the market, at least until the generic versions of Abraxane becomes available. In addition, we may also face competition from other products seeking approval in conjunction with gemcitabine and Abraxane including FOLFRINOX, a combination chemotherapy regimen of folic acid, 5-fluouracil, oxaliplatin and irinotecan, Rafael Pharma's defactinib/CPI-613, and Merrimack's istiratumab.

Duchenne Muscular Dystrophy

If approved and launched commercially to treat DMD, pamrevlumab is expected to face competition from drugs that have been approved in major markets such as the U.S., European Union, and Japan.

On September 19, 2016, the FDA approved Sarepta Therapeutics Inc.'s ("Sarepta") Exondys 51TM (eteplirsen). Exondys 51 is approved to treat patients who have a mutation of the dystrophin gene amenable to exon 51 skipping, representing approximately 13% of patients with DMD. In Europe, Sarepta received a negative opinion for its marketing application for eteplirsen from the EMA in September 2018. Sarepta has reported a full year Exondys 51 revenue of \$380 million in 2019. Sarepta's Vyondys 53TM (golodirsen) was approved by the FDA in December 2019 for patients with a confirmed genetic mutation that is amenable to exon 53 skipping, which accounts for approximately 8% of the DMD population. Sarepta's Amondys 45TM (casimersen) was approved by the FDA in February 2021 for patients with a confirmed genetic mutation that is amenable to exon 45 skipping, which accounts for approximately 8% of the DMD population.

PTC Therapeutics' product Translarna TM received a conditional approval in Europe in 2014, which was renewed in November 2016 with a request for a new randomized placebo-controlled 18-month study by the Committee for Medicinal Products for Human Use of the EMA; however, the FDA informed the sponsor in a complete response letter in October 2017, as well as in its response to PTC Therapeutics' appeal, that the FDA is unable to approve the application in its current form. While Translarna TM targets a different set of DMD patients from those targeted by Sarepta's Exondys 51®, it is also limited to a subset of patients who carry a specific mutation. Conversely, pamrevlumab is intended to treat DMD patients without limitation to type of mutation.

Pamrevlumab may also face competition from other drugs currently in clinical development in patient recruiting and enrollment in clinical trials, and, if approved, in commercialization. Examples of those compounds currently under clinical development are the drug candidates from Catabasis Pharmaceuticals, Santhera Pharmaceuticals, and Sarepta.

MANUFACTURE AND SUPPLY

We have historically and in the future plan to continue to enter into contractual arrangements with qualified third-party manufacturers to manufacture and package our products and product candidates. We believe that this manufacturing strategy enables us to more efficiently direct financial resources to the research, development and commercialization of product candidates rather than diverting resources to establishing a significant internal manufacturing infrastructure, unless there is additional strategic value for establishing manufacturing capabilities, such as in China. As our product candidates proceed through development, we explore or enter into longer term commercial supply agreements with key suppliers and manufacturers in order to meet the ongoing and planned clinical and commercial supply needs for ourselves and our partners. Our timing of entry into these agreements is based on the current development and commercialization plans.

Roxadustat

Roxadustat is a small-molecule drug manufactured from generally available commercial starting materials and chemical technologies and multipurpose equipment available from many third party contract manufacturers. We have entered into commercial supply arrangements with Shanghai
SynTheAll Pharmaceutical Co., Ltd. ("WuXi STA") and Catalent, Inc. ("Catalent") as our primary manufacturers of roxadustat drug substance (also
known as active pharmaceutical ingredient or "API") and roxadustat drug product, respectively. WuXi STA is located in China and currently
supplies our API globally except for China, for which it manufactures an intermediate to be further manufactured by FibroGen Beijing. WuXi STA
has passed inspections by several regulatory agencies, including the FDA and NMPA, and is Current Good Manufacturing Practice ("cGMP")
compliant. Catalent is located in the U.S. and supplies our drug product tablets globally except for Japan, where they are manufactured by Astellas,
and China, where they are manufactured by FibroGen Beijing. Catalent has passed several regulatory inspections, including by the FDA, and
manufactures commercial products for other clients.

In China, our Beijing facility received the Good Manufacturing Practice ("GMP") license for API and drug product. We are manufacturing drug product at our FibroGen Beijing manufacturing facility for commercial supply, but we are not currently manufacturing API at this facility. We are manufacturing API at our Cangzhou manufacturing facility, which has been fully qualified and licensed. We may also qualify a third party manufacturer to produce commercial API under the Marketing Authorization Holder System program.

Irix Pharmaceuticals, Inc.

In July 2002, we and IRIX Pharmaceuticals, Inc. ("IRIX"), a third party manufacturer, entered into a Letter of Agreement for IRIX Pharmaceuticals Single Source Manufacturing Agreement (the "Letter of Agreement"), in connection with a contract manufacturing arrangement for clinical supplies of HIF-PH inhibitors, including roxadustat. The Letter of Agreement contained a service agreement that included terms and schedule for the delivery of clinical materials and also included a term sheet for a single source agreement for the cGMP manufacture of HIF-PH inhibitors, including roxadustat. Specifically, pursuant to the Letter of Agreement, we and IRIX agreed to negotiate a single source manufacturing agreement that included a first right to negotiate a manufacturing contract for HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third party bids within 5%, and the exclusive right to manufacture extends for five years after approval of an NDA. Any agreement would provide that no minimum amounts would be specified until appropriate by forecast, that we and our commercialization partner would have the rights to contract with independent third parties that exceed IRIX's internal capabilities or in the event that we or our commercialization partner determines for reasons of continuity and security that such a need exists, provided that IRIX would supply a majority of the product if it is able to meet the requirements and the schedule required by us and our partner. Subsequent to the Letter of Agreement, IRIX and we have entered into several additional service agreements. IRIX has requested in writing that we honor the Letter of Agreement with respect to the single source manufacturing agreement. To date, we have offered to IRIX opportunities to bid for the manufacture of HIF-PH inhibitors, including roxadustat. In 2015, Patheon Pharmaceuticals Inc., a business unit of DPx Holdings B.V., acquired IRIX, and in 2017 ThermoFisher Scientific Inc. acquired Patheon

Pamrevlumab

To date, pamrevlumab has been manufactured using specialized biopharmaceutical process techniques under a clinical supply agreement with a qualified third party contract manufacturer, Boehringer Ingelheim. We have entered into a clinical and commercial supply agreement for the manufacture of pamrevlumab with Samsung Biologics Co., Ltd., which has passed several regulatory inspections, including by the FDA, and manufactures commercial products for other clients.

GOVERNMENT REGULATION

Our business activities and operations, including the clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing of our product candidates, among other things, are subject to extensive regulation by governmental authorities in the U.S., China, and other countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations, including in Europe and China, requires the expenditure of substantial time and financial resources. Compliance with environmental laws, rules, and regulations has not had, and is not expected to have, a material effect on our capital expenditures, results of operations, or competitive position, and we do not currently anticipate material capital expenditures for environmental control facilities.

Failure to comply with the applicable requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the applicable regulatory authority to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by FDA and the Department of Justice, or other governmental entities.

We cannot predict with certainty whether future costs of compliance with government regulations, including any changes thereto or reinterpretations thereof, will have a material impact on capital expenditures, earnings or the company's competitive position. Refer to the section of this Annual Report captioned "Item 1A. Risk Factors" for a discussion of these potential impacts.

U.S. Product Approval Process

In the U.S., the FDA regulates drugs and biological products, or biologics, under the Public Health Service Act, as well as the FDCA, which is the primary law for regulation of drug products. Both drugs and biologics are subject to the regulations and guidance implementing these laws. Pharmaceutical products are also subject to regulation by other governmental agencies, such as the Federal Trade Commission, the Office of Inspector General of the U.S. Department of Health and Human Services, the Consumer Product Safety Commission and the Environmental Protection Agency. The clinical testing, manufacturing, labeling, storage, distribution, record keeping, advertising, promotion, import, export and marketing, among other things, of our product candidates are subject to extensive regulation by governmental authorities in the U.S. and other countries. The steps required before a drug or biologic may be approved for marketing in the U.S. generally include:

- Preclinical laboratory tests and animal tests conducted under Good Laboratory Practices.
- The submission to the FDA of an IND for human clinical testing, which must become effective before each human clinical trial commence.
- Adequate and well-controlled human clinical trials to establish the safety and efficacy of the product and conducted in accordance with good clinical practices ("GCP").
- The submission to the FDA of an NDA, in the case of a small molecule drug product, or a BLA, in the case of a biologic product.
- FDA acceptance, review and approval of the NDA or BLA, as applicable.
- Satisfactory completion of an FDA inspection of the manufacturing facilities at which the product is made to assess compliance with cGMPs.

The testing and approval process requires substantial time, effort and financial resources, and the receipt and timing of any approval is uncertain. The FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to a potentially unacceptable health risk.

Preclinical studies include laboratory evaluations of the product candidate, as well as animal studies to assess the potential safety and efficacy of the product candidate. Preclinical studies must be conducted in compliance with FDA regulations regarding GLPs. The results of the preclinical studies, together with manufacturing information and analytical data, are submitted to the FDA as part of the IND, which includes the results of preclinical testing and a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase or phases of the clinical trial lends themselves to an efficacy determination. The IND will become effective automatically 30 days after receipt by the FDA, unless the FDA raises concerns or questions about the conduct of the trials as outlined in the IND prior to that time. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can proceed. The IND must become effective before clinical trials may be commenced.

Clinical trials involve the administration of the product candidates to healthy volunteers, or subjects, or patients with the disease to be treated under the supervision of a qualified principal investigator. Clinical trials must be conducted under the supervision of one or more qualified principal investigators in accordance with GCPs and in accordance with protocols detailing the objectives of the applicable phase of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Progress reports detailing the status of clinical trials must be submitted to the FDA annually. Sponsors must also timely report to the FDA serious and unexpected adverse events, any clinically important increase in the rate of a serious suspected adverse event over that listed in the protocol or investigator's brochure, or any findings from other studies or tests that suggest a significant risk in humans exposed to the product candidate. Further, the protocol for each clinical trial must be reviewed and approved by an independent institutional review board ("IRB"), either centrally or individually at each institution at which the clinical trial will be conducted. The IRB will consider, among other things, ethical factors, and the safety of human subjects and the possible liability of the institution.

Clinical trials are typically conducted in three sequential phases prior to approval, but the phases may overlap and different trials may be initiated with the same drug candidate within the same phase of development in similar or different patient populations. These phases generally include the following:

Phase 1. Phase 1 clinical trials represent the initial introduction of a product candidate into human subjects, frequently healthy volunteers. In Phase 1, the product candidate is usually tested for pharmacodynamic and pharmacokinetic properties such as safety, including adverse effects, dosage tolerance, absorption, distribution, metabolism and excretion.

Phase 2. Phase 2 clinical trials usually involve studies in a limited patient population to (1) evaluate the efficacy of the product candidate for specific indications, (2) determine dosage tolerance and optimal dosage and (3) identify possible adverse effects and safety risks.

Phase 3. If a product candidate is found to be potentially effective and to have an acceptable safety profile in Phase 2 studies, the clinical trial program will be expanded to Phase 3 clinical trials to further evaluate clinical efficacy, optimal dosage and safety within an expanded patient population at geographically dispersed clinical study sites.

Phase 4. Phase 4 clinical trials are conducted after approval to gain additional experience from the treatment of patients in the intended therapeutic indication and to document a clinical benefit in the case of drugs approved under accelerated approval regulations, or when otherwise requested by the FDA in the form of post-market requirements or commitments. Failure to promptly conduct any required Phase 4 clinical trials could result in withdrawal of approval.

The results of preclinical studies and clinical trials, together with detailed information on the manufacture, composition and quality of the product candidate, are submitted to the FDA in the form of an NDA (for a drug) or BLA (for a biologic), requesting approval to market the product. The application must be accompanied by a significant user fee payment. The FDA has substantial discretion in the approval process and may refuse to accept any application or decide that the data is insufficient for approval and require additional preclinical, clinical or other studies.

Review of Application

Once the NDA or BLA submission has been accepted for filing, which occurs, if at all, 60 days after submission, the FDA informs the applicant of the specific date by which the FDA intends to complete its review. This is typically 12 months from the date of submission. The review process is often extended by FDA requests for additional information or clarification. The FDA reviews NDAs and BLAs to determine, among other things, whether the proposed product is safe and effective for its intended use, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, strength, quality and purity. Before approving an NDA or BLA, the FDA may inspect the facilities at which the product is manufactured and will not approve the product unless the manufacturing facility complies with cGMPs and will also inspect clinical trial sites for integrity of data supporting safety and efficacy. During the approval process, the FDA also will determine whether a REMS, is necessary to assure the safe use of the product. If the FDA concludes a REMS is needed, the sponsor of the application must submit a proposed REMS; the FDA will not approve the application without an approved REMS, if required. A REMS can substantially increase the costs of obtaining approval. The FDA may also convene an advisory committee of external experts to provide input on certain review issues relating to risk, benefit and interpretation of clinical trial data. The FDA may delay approval of an NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The FDA may require post-marketing testing and surveillance to monitor safety or efficacy of a product. FDA will issue either an approval of the NDA or BLA or a complete response letter detailing the deficiencies and information required in order for reconsideration of the application.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act, certain drugs or biologics may obtain an additional six months of exclusivity in an indication, if the sponsor submits information requested in writing by the FDA ("Written Request"), relating to the use of the active moiety of the drug or biologic in children. The FDA may not issue a Written Request for studies on unapproved or approved indications or where it determines that information relating to the use of a drug or biologic in a pediatric population, or part of the pediatric population, may not produce health benefits in that population.

We have not received a Written Request for such pediatric studies with respect to our product candidates, although we may ask the FDA to issue a Written Request for studies in the future. To receive the six-month pediatric market exclusivity, we would have to receive a Written Request from the FDA, conduct the requested studies in accordance with a written agreement with the FDA or, if there is no written agreement, in accordance with commonly accepted scientific principles, and submit reports of the studies. A Written Request may include studies for indications that are not currently in the labeling if the FDA determines that such information will benefit the public health. The FDA will accept the reports upon its determination that the studies were conducted in accordance with and are responsive to the original Written Request, agreement, or commonly accepted scientific principles, as appropriate, and that the reports comply with the FDA's filing requirements.

In addition, the Pediatric Research Equity Act ("PREA") requires a sponsor to conduct pediatric studies for most drugs and biologicals, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must include the evaluation of the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA, on its own initiative or at the request of the sponsor, may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted by FDA if they believe that additional safety or effectiveness data in the adult population needs to be collected before the pediatric studies begin. After April 2013, the FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

Post-Approval Requirements

Even after approval, drugs and biologics manufactured or distributed pursuant to FDA approvals are subject to continuous regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA or BLA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

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In addition, entities involved in the manufacture and distribution of approved drugs and biologics are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may also result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- · Restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls.
- Fines, warning letters or holds on post-approval clinical trials.
- Refusal of the FDA to approve pending NDAs or BLAs or supplements to approved NDAs or BLAs, or suspension or revocation of
 product license approvals.
- Product seizure or detention, or refusal to permit the import or export of products.
- Injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Prescription Drug Marketing Act

The distribution of pharmaceutical products is subject to the Prescription Drug Marketing Act ("PDMA"), which regulates the distribution of drugs and drug samples at the federal level and sets minimum standards for the registration and regulation of drug distributors at the state level. Under the PDMA and state law, states require the registration of manufacturers and distributors who provide pharmaceuticals in that state, including in certain states manufacturers and distributors who ship pharmaceuticals into the state even if such manufacturers or distributors have no place of business within the state. The PDMA and state laws impose requirements and limitations upon drug sampling to ensure accountability in the distribution of samples. The PDMA sets forth civil and criminal penalties for violations of these and other provisions.

Federal and State Fraud and Abuse and Data Privacy and Security and Transparency Laws and Regulations

In addition to FDA restrictions on marketing of pharmaceutical products, federal and state healthcare laws restrict certain business practices in the biopharmaceutical industry. These laws include, but are not limited to, anti-kickback, false claims, data privacy and security, and transparency statutes and regulations.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for a statutory exception or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated. The intent standard under the Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act of 2010 (collectively "PPACA"), to a stricter intent standard such that a person or entity no longer needs to have actual knowledge of this statute or the specific intent to violate it in order to have committed a violation. In addition, PPACA codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act (discussed below). Further, civil monetary penalties statute imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment or approval to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses. The federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of, or payment for, healthcare benefits, items or services.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to business associates - independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act within the PPACA, and its implementing regulations, require that certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some states require the posting of information relating to clinical studies. In addition, California requires pharmaceutical companies to implement a comprehensive compliance program that includes a limit on expenditures for, or payments to, individual medical or health professionals. If our operations are found to be in violation of any of the health regulatory laws described above or any other laws that apply to us, we may be subject to penalties, including potentially significant criminal, civil and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion of products from reimbursement under government programs, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our products will be sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Pharmaceutical Coverage, Pricing and Reimbursement

In both domestic and foreign markets, our sales of any approved products will depend in part on the availability of coverage and adequate reimbursement from third-party payors. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. Patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our products. Sales of our products will therefore depend substantially, both domestically and abroad, on the extent to which the costs of our products will be paid by third-party payors. These third-party payors are increasingly focused on containing healthcare costs by challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the coverage and reimbursement status of newly approved healthcare product candidates. The market for our products and product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Because each third-party payor individually approves coverage and reimbursement levels, obtaining coverage and adequate reimbursement is a time-consuming, costly and sometimes unpredictable process. We may be required to provide scientific and clinical support for the use of any product to each third-party payor separately with no assurance that approval would be obtained, and we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of our products. This process could delay the market acceptance of any product and could have a negative effect on our future revenues and operating results. We cannot be certain that our products and our product candidates will be considered cost-effective. Because coverage and reimbursement determinations are made on a payor-by-payor basis, obtaining acceptable coverage and reimbursement from one payor does not guarantee that we will obtain similar acceptable coverage or reimbursement from another payor. If we are unable to obtain coverage of, and adequate reimbursement and payment levels for, our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer them and patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition and future success.

In addition, in many foreign countries, particularly the countries of the European Union and China, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of a company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

Healthcare Reform

In the U.S. and foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations as we begin to directly commercialize our products. In particular, there have been and continue to be a number of initiatives at the U.S. federal and state level that seek to reduce healthcare costs. If a drug product is reimbursed by Medicare or Medicaid, pricing and rebate programs must comply with, as applicable, the Medicaid rebate requirements of the Omnibus Budget Reconciliation Act of 1990, as amended, and the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA"). The MMA imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities that provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain from non-governmental payors. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payors.

Moreover, on November 27, 2013, the federal Drug Supply Chain Security Act was signed into law, which imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new federal legislation, manufacturers will be required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, and notification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Furthermore, political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental change. Initiatives to reduce the federal budget and debt and to reform healthcare coverage are increasing cost-containment efforts. We anticipate that Congress, state legislatures and the private sector will continue to review and assess alternative healthcare benefits, controls on healthcare spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, the creation of large insurance purchasing groups, price controls on pharmaceuticals and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit or eliminate our spending on development projects and affect our ultimate profitability.

Under the Medicare Improvements for Patients and Providers Act ("MIPPA"), a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the End-Stage Renal Disease Prospective Payment System (the "ESRD PPS") bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by the CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage. It is unknown whether roxadustat, if approved in the U.S., will be included in the payment bundle or the timing of inclusion. Under MIPPA, agents that have no IV equivalent in the bundle are currently expected to be excluded from the bundle until 2025. If roxadustat were included in the bundle, it may reduce the price that could be charged for roxadustat, and therefore potentially limit our profitability. Based on roxadustat's differentiated mechanism of action and therapeutic effects, and discussions with our collaboration partner, we currently believe that roxadustat might not initially be included in the bundle and would instead be eligible for a Transitional Drug Add-on Payment Adjustment ("TDAPA") for a 24-month period. At the 24-month mark, CMS would determine if the TDAPA period should be extended for roxadustat or ended. When the TDAPA period ends, CMS will determine if roxadustat should be included in the bundle and, if so, what changes to the ESRD PPS reimbursement should be made. If roxadustat is included in the ESRD PPS bundle, it may have an impact on roxadustat pricing within Dialysis Organizations. If roxadustat is not included in the bundle after the TDAPA period, and would therefore be reimbursed outside of the bundle, it may potentially limit further market penetration of roxadustat.

In March 2010, PPACA was signed into law. PPACA has the potential to substantially change the way healthcare is financed by both governmental and private insurers. Among other cost containment measures, PPACA established: an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents; revised the methodology by which rebates owed by manufacturers to the state and federal government for covered outpatient drugs under the Medicaid Drug Rebate Program are calculated; increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; and extended the Medicaid Drug Rebate program to utilization of prescriptions of individuals enrolled in Medicaid managed care organizations. There remain judicial and Congressional challenges to certain aspects of the PPACA. The U.S. Supreme Court is currently reviewing the constitutionality of the PPACA, but it is unknown when a decision will be reached. It is unclear how the U.S. Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the PPACA. In the future, there may continue to be additional proposals relating to the reform of the U.S. healthcare system, some of which could further limit the prices we are able to charge for our products, or the amounts of reimbursement available for our products. If future legislation were to impose direct governmental price controls and access restrictions, it could have a significant adverse impact on our business. Managed care organizations, as well as Medicaid and other government agencies, continue to seek price discounts.

Further, in the U.S. there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives.

Some states have implemented, and other states are considering, price controls or patient access constraints under the Medicaid program, and some states are considering price-control regimes that would apply to broader segments of their populations that are not Medicaid-eligible. Due to the volatility in the current economic and market dynamics, we are unable to predict the impact of any unforeseen or unknown legislative, regulatory, payor or policy actions, which may include cost containment and healthcare reform measures. Such policy actions could have a material adverse impact on our profitability.

Approval Process and Other Regulation in China

The pharmaceutical industry in China is highly regulated. The primary regulatory authority is the NMPA, including its provincial and local branches. As a developer, manufacturer and supplier of drugs, we are subject to regulation and oversight by the NMPA and its provincial and local branches. The Drug Administration Law of China provides the basic legal framework for the administration of the production and sale of pharmaceuticals in China and covers the manufacturing, distributing, packaging, pricing and advertising of pharmaceutical products. Its implementing regulations set forth detailed rules with respect to the administration of pharmaceuticals in China. In addition, we are, and we will be, subject to other Chinese laws and regulations that are applicable to business operators, manufacturers and distributors in general.

Pharmaceutical Clinical Development

A new drug must be approved by the NMPA before it can be manufactured and marketed for sale. To obtain NMPA approval, the applicant must conduct clinical trials, which must be approved by the NMPA and are subject to the NMPA's supervision and inspection. There are four phases of clinical trials. Application for registration of new drugs requires completion of Phase 1, 2 and 3 of clinical trials, similar to the U.S. In addition, the NMPA may require the conduct of Phase 4 studies as a condition to approval.

Phase 4 studies are post-marketing studies to assess the therapeutic effectiveness of and adverse reactions to the new drug, including an evaluation of the benefits and risks, when used among the general population or specific groups, with findings used to inform adjustments to dosage, among other things.

NDA and Approval to Market

China requires approval of the NDA as well as the manufacturing facility before a drug can be marketed in China. Approval and oversight are performed at national and provincial levels of the NMPA, involve multiple agencies and consist of various stages of approval.

Under the applicable drug registration regulations, drug registration applications are divided into three different types, namely Domestic NDA, Domestic Generic Drug Application, and Imported Drug Application. Drugs fall into one of three categories, namely chemical medicine, biological product or traditional Chinese or natural medicine.

Our roxadustat NDA for treatment of CKD anemia was submitted by FibroGen Beijing as a domestic entity under the Domestic Class 1 designation, which refers to a new drug that has never been marketed in any country.

Our NDA package in China contained information similar to what is necessary for a U.S. NDA, including preclinical data, clinical data, technical data on API and drug product, and related stability data. We are currently performing a safety study of 2,000 patients who will be treated for 52 weeks as part of our post-approval commitment to the NMPA.

Shortly before NDA approval, FibroGen Beijing conducted a three-batch validation campaign, one of which was observed onsite by the NMPA. Following the successful completion of the validation campaign and associated inspection, FibroGen Beijing was granted a cGMP certification for the commercial production of roxadustat at our Beijing manufacturing facility. We are using our FibroGen Beijing manufacturing facility for commercial supply of drug product. Our Cangzhou manufacturing facility has been fully qualified and licensed for manufacture of roxadustat API for the China market, and we will continue to use this facility for commercial supply. We may also qualify a third party manufacturer to produce commercial API under the Marketing Authorization Holder System program.

Pricing, Reimbursement, Hospital Listing, and Tendering

Please see the discussion above in the section "Roxadustat for the Treatment of Anemia in Chronic Kidney Disease in China."

Foreign Regulation Outside of China

In order to market any product outside of the U.S., we would need to comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, manufacturing, marketing authorization, commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we would need to obtain the necessary approvals by the comparable foreign regulatory authorities before we can commence clinical trials or marketing of the product in foreign countries and jurisdictions. Although many of the issues discussed above with respect to the U.S. apply similarly in the context of other countries we are seeking approval in, including Europe and China, the approval process varies between countries and jurisdictions and can involve different amounts of product testing and additional administrative review periods. For example, in Europe and in China, a sponsor must submit a clinical trial application ("CTA"), much like an IND prior to the commencement of human clinical trials. A CTA must be submitted to each national health authority and an independent ethics committee.

For other countries outside of the European Union, such as China and the countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing, and reimbursement vary from country to country. The time required to obtain approval in other countries and jurisdictions might differ from or be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory approval process in other countries.

Regulatory Exclusivity for Approved Products

U.S. Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. The patent term restoration period is generally one-half the time between the effective date of an initial IND and the submission date of an NDA or BLA, plus the time between the submission date of the NDA or BLA and the approval of that product candidate application. Patent term restoration cannot, however, extend the remaining term of a patent beyond a total of 14 years from the product's approval date. In addition, only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for any patent term extension or restoration. In the future, we expect to apply for restoration of patent term for patents relating to each of our product candidates in order to add patent life beyond the current expiration date of such patents, depending on the length of the clinical trials and other factors involved in the filing of the relevant NDA or BLA.

Market exclusivity provisions under the FDCA can also delay the submission or the approval of certain applications of companies seeking to reference another company's NDA or BLA. The Hatch-Waxman Act provides a 5-year period of exclusivity to any approved NDA for a product containing a NCE never previously approved by FDA either alone or in combination with another active moiety. No application or abbreviated NDA directed to the same NCE may be submitted during the 5-year exclusivity period, except that such applications may be submitted after four years if they contain a certification of patent invalidity or non-infringement of the patents listed with the FDA by the innovator NDA.

Biologic Price Competition and Innovation Act

The Biologics Price Competition and Innovation Act of 2009 ("BPCIA"), established an abbreviated pathway for the approval of biosimilar and interchangeable biological products. The abbreviated regulatory approval pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on similarity to an existing branded product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement to one of the patents listed with the FDA by the innovator BLA holder. The BPCIA is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and interpretation are subject to uncertainty.

Orphan Drug Act

Pamrevlumab has received orphan drug designation in IPF, LAPC, and DMD in the U.S. Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biological product intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects more than 200,000 individuals in the U.S. there is no reasonable expectation that the cost of developing and making a drug product available in the U.S. for this type of disease or condition will be recovered from sales of the product. Orphan product designation must be requested before submitting an NDA. After the FDA grants orphan product designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

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If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug or biological product as defined by the FDA or if our drug candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity in any indication.

The EMA has granted Orphan Medicinal Product Designation to pamrevlumab for the treatment of DMD. Orphan Medicinal Product Designation status in Europe has similar but not identical benefits in that jurisdiction.

Products receiving orphan designation in Europe can receive ten years of market exclusivity, during which time no similar medicinal product for the same indication may be placed on the market. The ten-year market exclusivity may be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan designation; for example, if the product is sufficiently profitable not to justify maintenance of market exclusivity. Additionally, marketing authorization may be granted to a similar product for the same indication at any time if the second applicant can establish that its product, although similar, is safer, more effective or otherwise clinically superior; the initial applicant consents to a second orphan medicinal product application; or the initial applicant cannot supply enough orphan medicinal product. An orphan product can also obtain an additional two years of market exclusivity in Europe for pediatric studies. No extension to any supplementary protection certificate can be granted on the basis of pediatric studies for orphan indications.

Foreign Country Data Exclusivity

Europe also provides opportunities for additional market exclusivity. For example, in Europe, upon receiving marketing authorization, an NCE generally receives eight years of data exclusivity and an additional two years of market exclusivity. If granted, data exclusivity prevents regulatory authorities in Europe from referencing the innovator's data to assess a generic application. During the additional two-year period of market exclusivity, a generic marketing authorization can be submitted, and the innovator's data may be referenced, but no generic product can be marketed until the expiration of the market exclusivity.

In China, there is also an opportunity for data exclusivity for a period of six years for data included in an NDA applicable to a NCE. According to the Implementing Regulations of the PRC Drug Administration Law, the Chinese government protects undisclosed data from drug studies and prevents the approval of an application made by another company that uses the undisclosed data for the approved drug. In practice, the NMPA has not established an effective mechanism to enforce data exclusivity. The NMPA issued a draft regulation on regulatory data protection on April 25, 2018 for public comments but this draft regulation has yet to be finalized and implemented.

In addition, if an approved drug manufactured in China qualifies as an innovative drug or an improved new drug before December 1, 2019, such drugs will be eligible for a monitoring surveillance period for up to five years. During this post-marketing observation period, the NMPA will not accept marketing authorization applications filed by another company for the same product. Nor will the NMPA approve marketing authorization applications filed by another company to produce, change dosage form of or import the drug while the innovative or improved new drug is under observation for the purpose of protecting public health. The approved manufacturer is required to provide an annual report to the regulatory department of the province, autonomous region or municipality directly under the central government where it is located.

Each of the data exclusivity period and the observation period runs from the date of approval for production of the NCE or innovative or improved new drug, as the case may be.

INTELLECTUAL PROPERTY

Our success depends in part upon our ability to obtain and maintain patent and other intellectual property protection for our product candidates including compositions-of-matter, dosages, and formulations, manufacturing methods, and novel applications, uses and technological innovations related to our product candidates and core technologies. We also rely on trade secrets, know-how and continuing technological innovation to further develop and maintain our competitive position.

Our policy is to seek to protect our proprietary position by, among other methods, filing U.S. and foreign patent applications related to our proprietary technologies, inventions and any improvements that we consider important to the development and implementation of our business and strategy. Our ability to maintain and solidify our proprietary position for our products and technologies will depend, in part, on our success in obtaining and enforcing valid patent claims. Additionally, we may benefit from a variety of regulatory frameworks in the U.S., Europe, China, and other territories that provide periods of non-patent-based exclusivity for qualifying drug products. *Refer to "Government Regulation - Regulatory Exclusivity for Approved Products."*

We cannot ensure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications that may be filed by us in the future, nor can we ensure that any of our existing or subsequently granted patents will be useful in protecting our drug candidates, technological innovations, and processes. Additionally, any existing or subsequently granted patents may be challenged, invalidated, circumvented or infringed. We cannot guarantee that our intellectual property rights or proprietary position will be sufficient to permit us to take advantage of current market trends or otherwise to provide or protect competitive advantages. Furthermore, our competitors may be able to independently develop and commercialize similar products, or may be able to duplicate our technologies, business model, or strategy, without infringing our patents or otherwise using our intellectual property.

Our extensive worldwide patent portfolio includes multiple granted and pending patent applications relating to roxadustat and pamrevlumab. Currently granted patents relating to composition-of-matter for roxadustat and for pamrevlumab are expected, for each product candidate, to expire in 2024 or 2025, in each case exclusive of any patent term extension that may be available. U.S. and foreign patents relating to crystalline forms of roxadustat are expected to expire in 2033, exclusive of any extension. Additional patents and patent applications relating to manufacturing processes, formulations, and various therapeutic uses, including treatment of specific indications and improvement of clinical parameters, provide further protection for product candidates.

The protection afforded by any particular patent depends upon many factors, including the type of patent, scope of coverage encompassed by the granted claims, availability of extensions of patent term, availability of legal remedies in the particular territory in which the patent is granted, and validity and enforceability of the patent. Changes in either patent laws or in the interpretation of patent laws in the U.S. and other countries could diminish our ability to protect our inventions and to enforce our intellectual property rights. Accordingly, we cannot predict with certainty the enforceability of any granted patent claims or of any claims that may be granted from our patent applications.

The biotechnology and pharmaceutical industries are characterized by extensive litigation regarding patents and other intellectual property rights. Our ability to maintain and solidify our proprietary position for our products and core technologies will depend on our success in obtaining effective claims and enforcing those claims once granted. We have been in the past and are currently involved in various legal proceedings with respect to our patents and patent applications and may, as a result of our extensive portfolio, be involved in such proceedings in the future. Additionally, we may claim that a third party infringes our intellectual property or a third party may claim that we infringe its intellectual property. Such legal proceedings may be associated with significant expenses, damages, attorneys' fees, costs of proceedings and experts' fees, and management and employees may be required to spend significant time in connection with these actions.

Because of the extensive time required for clinical development and regulatory review of a product candidate we may develop, it is possible that any patent related to our product candidates may expire before any of our product candidates can be commercialized, or may remain in force for only a short period of time following commercialization, thereby reducing the advantage afforded by any such patent.

The patent positions for our most advanced programs are summarized below.

Roxadustat Patent Portfolio

Our roxadustat patent portfolio includes multiple granted U.S. patents offering protection for roxadustat, including protection for roxadustat composition-of-matter, for pharmaceutical compositions containing roxadustat, and for methods for treating anemia using roxadustat or its analogs. Exclusive of any patent term extension, the granted U.S. patents relating to the composition-of-matter of roxadustat are due to expire in 2024 or 2025, and granted foreign patents are due to expire in 2024. U.S. and foreign patents relating to crystalline forms of roxadustat are due to expire in 2033, and U.S. and foreign patents relating to photostable formulations of roxadustat are due to expire in 2034.

In 2020, oppositions were filed against our European Patent No. 2872488 (the "'488 Patent"), which claims a crystalline form of roxadustat, and our European Patent No. 3003284 (the "'284 Patent"), which claims photostable formulations of roxadustat. Final resolution of the opposition proceedings will take time and we cannot be assured that all or any claims will remain.

We believe that, if roxadustat is approved, a full five-year patent term extension under the Hatch-Waxman act will be available for a granted U.S. patent relating to roxadustat, which extension would expire in 2029 or 2030, depending on the patent extended. Refer to "Government Regulation - Regulatory Exclusivity for Approved Products - U.S. Patent Term Restoration."

We also hold various U.S. and foreign granted patents and pending patent applications directed to manufacturing processes, formulations, and methods for use of roxadustat.

Roxadustat China Patent Portfolio

Our roxadustat China patent portfolio includes granted patents covering roxadustat composition-of-matter, pharmaceutical compositions, methods of use, and manufacturing processes for roxadustat, as well as medicaments containing roxadustat for treating anemia and other conditions. Patents relating to roxadustat composition-of-matter and crystalline forms are due to expire in 2024 and 2033, respectively.

HIF Anemia-Related Technologies Patent Portfolio

We also have an extensive worldwide patent portfolio providing broad protection for proprietary technologies relating to the treatment of anemia and associated conditions. This portfolio currently contains granted patents and pending patent applications providing exclusivity for use of compounds falling within various and overlapping classes of HIF-PH inhibitors to achieve various therapeutic effects.

Various legal challenges have been initiated against this portfolio in several territories, including in Europe, the United Kingdom, Canada, and Japan. Regardless of the final outcome of any such actions, the potential narrowing or revocation of any of these patents does not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia in these or in other territories. A settlement has been reached in the litigation in Canada, resulting in the discontinuance of the action and leaving FibroGen's Canadian patents valid and enforceable.

In April 2020, in response to an invalidation action brought against certain of our United Kingdom patents by Akebia, the United Kingdom court handed down a decision invalidating United Kingdom designations of European Patent Nos. 1463823, 1633333, 2298301, 2322153, and 2322155. The United Kingdom designation to European Patent No. 2289531 was held to be valid in amended form, but not infringed by Akebia. We and our partner Astellas have filed an appeal of the decision in the United Kingdom Court of Appeal.

Pamrevlumab Patent Portfolio

Our pamrevlumab patent portfolio includes U.S. patents providing composition-of-matter protection for pamrevlumab and related antibodies, and for methods of using such in the treatment of fibroproliferative disorders, including IPF, liver fibrosis, and pancreatic cancer. Exclusive of any patent term extension, U.S. patents relating to pamrevlumab composition-of-matter are due to expire in 2024 or 2025. Corresponding foreign patents are due to expire, exclusive of any patent term extension, in 2024.

We believe that, if pamrevlumab is approved, a full five-year patent term extension under the Hatch-Waxman act will be available for a granted patent relating to pamrevlumab, which extension would expire in 2029 or 2030, depending on the patent extended.

We also hold additional granted U.S. and foreign patents and pending patent applications directed to the use of pamrevlumab to treat IPF, DMD, pancreatic cancer, liver fibrosis, and other disorders.

Trade Secrets and Know-How

In addition to patents, we rely upon proprietary trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality and other terms in agreements with our commercial partners, collaboration partners, consultants and employees. Such agreements are designed to protect our proprietary information, and may also grant us ownership of technologies that are developed through a relationship with a third party, such as through invention assignment provisions. Agreements may expire and we could lose the benefit of confidentiality, or our agreements may be breached and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors.

To the extent that our commercial partners, collaboration partners, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

In-Licenses

Dana-Farber Cancer Institute

Effective March 2006, we entered into a license agreement with the Dana-Farber Cancer Institute ("DFCI"), under which we obtained an exclusive license to certain patent applications, patents and biological materials for all uses. The patent rights relate to inhibition of prolyl hydroxylation of the alpha subunit of hypoxia-inducible factor (HIFα), and include granted U.S. and foreign patents due to expire in 2022, exclusive of possible patent term extension. The licensed patents relate to use of HIF-PH inhibitors such as roxadustat.

Under the DFCI agreement, we are obligated to pay DFCI for past and ongoing patent prosecution expenses for the licensed patents. We are also obligated to pay DFCI annual maintenance fees, development milestone payments of up to \$425,000, sales milestone payments of up to \$3 million, and a sub-single-digit royalty on net sales by us or our affiliates or sublicensees of products that are covered by the licensed patents or incorporate the licensed biological materials. In addition, each sublicense we grant is subject to a one-time fixed amount payment to DFCI.

The agreement, along with any ongoing payment obligations, will continue in effect until the expiration of all licensed patents on a country-by-country basis, or, if there is no patent covering a licensed product incorporating the licensed biological materials, until 20 years after the effective date of the agreement. DFCI may terminate the agreement for our uncured material breach, if we cease to carry on our business and development activities with respect to all licensed products, if we fail to comply with our insurance obligations, or if we are convicted of a felony related to the manufacture, use, sale or importation of licensed products. We may terminate the agreement at any time on prior written notice to DFCI.

University of Miami

In May 1997, we entered into a license agreement with the University of Miami (the "University"), amended in July 1999, under which we obtained an exclusive, worldwide license to certain patent applications and patents for all uses. The current patent rights consist of a U.S. patent that relates to antibodies that specifically bind to biologically active fragments of CTGF, and is due to expire in 2022, exclusive of any patent term extension or adjustment that may be available. The licensed patent relates to pamrevlumab and related products.

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Under the University agreement, we are obligated to pay for all ongoing patent expenses for the licensed patent. We were also obligated to pay an upfront licensing fee of \$21,500, all of which has been paid, and development milestone payments of up to \$450,000, of which \$150,000 has been paid, as well as an additional milestone payment, in the low hundreds of thousands of dollars, for each new indication for which we obtain approval for a licensed product, and a single digit royalty, subject to certain reductions, on net sales of licensed products by us or our affiliates or sublicensees.

The agreement, along with any ongoing payment obligations, will continue in effect until the expiration of all licensed patents, on a country-by-country basis. The University may terminate the agreement for our uncured material breach or bankruptcy. We may terminate the agreement for the University's uncured material breach or at any time on prior written notice to the University.

Bristol-Myers Squibb Company (Medarex, Inc.)

Effective July 9, 1998 and as amended on June 30, 2001 and January 28, 2002, we entered into a research and commercialization agreement with Medarex, Inc. and its wholly-owned subsidiary GenPharm International, Inc. (now, collectively, part of Bristol-Myers Squibb Company ("Medarex")) to develop fully human monoclonal antibodies for potential anti-fibrotic therapies. Under the agreement, Medarex was responsible for using its proprietary immunizable transgenic mice ("HuMAb-Mouse technology") during a specified research period (the "Research Period"), to produce fully human antibodies against our proprietary antigen targets, including CTGF, for our exclusive use.

The agreement granted us an option to obtain an exclusive worldwide, royalty-bearing, commercial license to develop antibodies derived from Medarex's HuMAb-Mouse technology, for use in the development and commercialization of diagnostic and therapeutic products. In December 2002, we exercised that option with respect to twelve antibodies inclusive of the antibody from which pamrevlumab is derived. We granted back to Medarex an exclusive, worldwide, royalty-free, perpetual, irrevocable license, with the right to sublicense, to certain inventions created during the parties' research collaboration, with such license limited to use by Medarex outside the scope of our licensed antibodies.

As a result of the exercise of our option to obtain the commercial license, Medarex is precluded from:

- (i) knowingly using any technology involving immunizable transgenic mice containing unrearranged human immunoglobulin genes with any of our antigen targets that were the subject of the agreement,
- (ii) granting to a third party a commercial license that covers such antigen targets or those antibodies derived by Medarex during the Research Period, and
- (iii) using any antibodies derived by Medarex during the Research Period, except as permitted under the agreement for our benefit or to prosecute patent applications in accordance with the agreement.

Medarex retained ownership of the patent rights relating to certain mice, mice materials, antibodies and hybridoma cell lines used by Medarex in connection with its activities under the agreement, and Medarex also owns certain claims in patents covering inventions that arise during the Research Period, which claims are directed to (i) compositions of matter (e.g., an antibody) except formulations of antibodies for therapeutic or diagnostic use, or (ii) methods of production. We own the patent rights to any inventions that arise during the Research Period that relate to antigens, as well as claims in patents covering inventions directed to (a) methods of use of an antibody, or (b) formulations of antibodies for therapeutic or diagnostic use. Upon exercise of our option to obtain the commercial license, we obtained the sole right but not obligation to control prosecution of patents relating solely to the licensed antibodies or products. Medarex has back-up patent prosecution rights in the event we decline to further prosecute or maintain such patents.

In addition to research support payments by us to Medarex during the Research Period, and an upfront commercial license fee in the form of 181,819 shares of FibroGen Series D Convertible Preferred Stock paid upon exercise of our option, we committed development-related milestone payments of up to \$11 million per therapeutic product containing a licensed antibody, and we have paid a \$1 million development-related milestone, in the form of 133,333 shares of FibroGen Series G Convertible Preferred Stock, and a cash payment of \$2 million, for pamrevlumab to date. At our election, the remaining milestone payments may be paid in common stock of FibroGen, Inc., or cash.

With respect to our sales and sales by our affiliates, the agreement also requires us to pay Medarex low single-digit royalties for licensed therapeutic products and low double-digit royalties plus certain capped sales-based bonus royalties for licensed diagnostic products. With respect to sales of licensed products by a sublicensee, we may elect to pay the foregoing royalties based on our sublicensee's sales, or a percentage (in the high-teens) of all payments received by us from such sublicensee. We are also required to reimburse Medarex any pass-through royalties, if any, payable under Medarex's upstream license agreements with Medical Research Council and DNX. Royalties payable by us under the agreement are on a licensed product-by-licensed product and country-by-country basis and subject to reductions in specified circumstances, and royalties are payable for a period until either expiration of patents covering the applicable licensed product or a specified number of years following the first commercial sale of such product in the applicable country.

Unless earlier terminated, the agreement will continue in effect for as long as there are royalty payment obligations by us or our sublicensees. Either party may terminate the agreement for certain material breaches by the other party, or for bankruptcy, insolvency or similar circumstances. In addition, we may also terminate the agreement for convenience upon written notice.

Third Party Filings

Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing products. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in granted patents that use of our product candidates or proprietary technologies may infringe.

If a third party claims that we infringe its intellectual property rights, we may face a number of issues, including but not limited to, litigation expenses, substantial damages, attorney fees, injunction, royalty payments, cross-licensing of our patents, redesign of our products, or processes and related fees and costs.

We may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that our products, product candidates, and/or proprietary technologies infringe their intellectual property rights. If one of these patents were to be found to cover our products, product candidates, proprietary technologies, or their uses, we could be required to pay damages and could be restricted from commercializing our products, product candidates or using our proprietary technologies unless we obtain a license to the patent. A license may not be available to us on acceptable terms, if at all. In addition, during litigation, the patent holder might obtain a preliminary injunction or other equitable right, which could prohibit us from making, using or selling our products, technologies, or methods.

HUMAN RESOURCES

We had a total of 599 employees at FibroGen as of January 31, 2021. None of our U.S. employees are represented by a labor union. The employees of FibroGen Beijing are represented by a labor union under the China Labor Union Law. None of our employees have entered into a collective agreement with us.

We are highly committed to building a diverse, committed, and impassioned team to deliver innovative therapies to patients facing serious unmet medical needs. In 2020 we developed and approved a new Corporate Vision Statement and Values through the participation and input of many staff across the organization. One of these core values is "Respect for People" which includes a strong commitment to build a culture of inclusiveness and equality and foster a culture of individual growth and an environment of continued learning.

In 2020, we conducted a company-wide employee engagement survey. We had an overall participation rate by employees of 86% with over 90% of respondents reporting that they felt engaged around our core values of excellence, respect for people, integrity, and empowerment. Both of these scores significantly exceed normative industry participation and engagement benchmarks.

The biotechnology industry is an extremely competitive labor market and recruiting and retaining employees is critical to the continued success of our business. We focus on recruiting, retaining, and developing employees from a diverse range of backgrounds to conduct our research, development, commercialization, and administrative activities.

We consistently review and evaluate our compensation and employee benefits practices to ensure that we recruit and retain a highly trained and diverse workforce. This includes comprehensive medical and income protection, such as life insurance and retirement savings programs. In addition to coaching and internal growth and promotion opportunities, we provide employees access to over 5,000 developmental classes and programs through a learning management system.

In 2020 we deployed a state-of-art, human capital management system that will allow us to significantly expand our capabilities to develop and assess our employees. This system will also allow us to build comprehensive development and succession plans at all levels in the organization to ensure that we have a strong pipeline of highly trained employees. We also invested in health and safety measures for our employees who must work in the offices and labs during the COVID-19 pandemic.

We are committed to diversity, equity and inclusion. On our Board of Directors: five of our twelve members are women and/or from minority racial and ethnic groups. As of January 31, 2021, women represented 54% of our global workforce and 27% of our global leadership (VP and above). As of January 31, 2021, 57% of our U.S. workforce, and 16% of our U.S. leadership (VP and above), were from minority racial and ethnic groups.

In addition to furthering our investments in our human resources, we plan on continuing our efforts in 2021 in critical environmental, social, and governance areas.

FACILITIES

Our corporate and research and development operations are located in San Francisco, California, where we lease approximately 234,000 square feet of office and laboratory space with approximately 35,000 square feet subleased. The lease for our San Francisco headquarters expires in 2023. We also lease approximately 67,000 square feet of office and manufacturing space in Beijing, China, and multiple office spaces in Beijing and Shanghai, China. Our leases in China expire in 2023. We have constructed a commercial manufacturing facility of approximately 5,500 square meters in Cangzhou, China, on approximately 33,000 square meters of land. Our right to use such land expires in 2068. We believe our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

AVAILABLE INFORMATION

Our internet website address is www.fibrogen.com. In addition to the information about us and our subsidiaries contained in this Annual Report, information about us can be found on our website. The information contained on, or that can be accessed through, our website is not part of, and is not incorporated into, this Annual Report.

Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge through our website as soon as reasonably practicable after they are electronically filed with or furnished to the Securities and Exchange Commission ("SEC"). Additionally the SEC maintains an internet site that contains reports, proxy and information statements and other information. The address of the SEC's website is www.sec.gov.

CORPORATE INFORMATION

Our headquarters are located at 409 Illinois Street, San Francisco, California 94158 and our telephone number is (415) 978-1200. Our website address is www.FibroGen.com.

Our subsidiaries consist of the following: 1) FibroGen Europe Oy, a majority owned entity incorporated in Finland in 1996; 2) Skin Sciences, Inc., a majority owned entity incorporated in the State of Delaware in 1995; 3) FibroGen International (Cayman) Limited, a majority owned entity incorporated in the Cayman Islands in 2011; 4) FibroGen China Anemia Holdings Ltd., a majority owned entity incorporated in the Cayman Islands in 2012; 5) FibroGen International (Hong Kong) Limited, a majority owned entity incorporated in Hong Kong in 2011; 6) FibroGen (China) Medical Technology Development Co., Ltd., a majority owned entity incorporated in China in 2011; and 7) Beijing Falikang Pharmaceutical Co. Ltd., an unconsolidated variable interest entity incorporated in China in 2020.

"FibroGen," the FibroGen logo and other trademarks or service marks of FibroGen, Inc. appearing in this Annual Report are the property of FibroGen, Inc. This Annual Report contains additional trade names, trademarks and service marks of others, which are the property of their respective owners. We do not intend our use of display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

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ITEM 1A. RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below in addition to the other information included or incorporated by reference in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes and "Management's Discussion and Analysis of Financial Condition and Results of Operations," before deciding whether to invest in our common stock. The occurrence of any of the events or developments described below could harm our business, financial condition, results of operations and growth prospects. In such an event, the market price of our common stock could decline, and you may lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our business operations.

Risks Related to the Development and Commercialization of Our Product Candidates

We are substantially dependent on the success of our lead product, roxadustat, and our second compound in development, pamrevlumab.

To date, we have invested a substantial portion of our efforts and financial resources in the research and development of roxadustat and pamrevlumab. While we have received approval of our New Drug Applications ("NDA") for roxadustat in the People's Republic of China ("China"), Japan, and Chile for chronic kidney disease ("CKD") anemia for patients on dialysis and not on dialysis, we and our partners will need to make substantial additional investments in the development and commercialization of roxadustat worldwide and in various indications. Our near-term prospects, including maintaining our existing collaborations with Astellas Pharma Inc. ("Astellas") and AstraZeneca AB ("AstraZeneca"), will depend heavily on successful development and commercialization of roxadustat, including obtaining additional regulatory approvals for the commercialization of roxadustat for anemia associated with CKD.

Our other lead product candidate, pamrevlumab, is currently in clinical development for idiopathic pulmonary fibrosis ("IPF"), pancreatic cancer, and Duchenne muscular dystrophy ("DMD"). Pamrevlumab requires substantial further development and investment and we do not have a collaboration partner for support of this compound. In addition, pamrevlumab is a monoclonal antibody, which may require greater financial resources than for our small molecule, roxadustat.

As a company, we have limited commercialization experience, and the time and resources to develop such experience are significant. If we fail to achieve and sustain commercial success for roxadustat with our collaboration partners, our business would be harmed.

We do not have a sales or marketing infrastructure and have limited experience in the sales, marketing or distribution of pharmaceutical products in any country. To achieve commercial success for any product for which we obtain marketing approval, we will need to establish sales and marketing capabilities or make and maintain our existing arrangements with third parties to perform these services at a level sufficient to support our commercialization efforts.

To the extent that we would undertake sales and marketing of any of our products directly, there are risks involved with establishing our own sales, marketing and distribution capabilities. Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future products;
- our inability to effectively manage geographically dispersed commercial teams;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent commercial organization.

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With respect to roxadustat, we are dependent on the commercialization capabilities of our collaboration partners, AstraZeneca and Astellas. If either such partner were to terminate its agreement with us, we would have to commercialize on our own or with another third party. We will have limited control over the commercialization efforts of such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products, if any, effectively. If they are not successful in commercializing our product candidates, our business and financial condition would suffer.

Commercializing roxadustat requires us to establish commercialization systems, including but not limited to, medical affairs, pharmacovigilance, supply-chain, and distribution capabilities to perform our portion of the collaborative efforts. These efforts require resources and time. If we, along with Astellas and AstraZeneca, are not successful in our marketing, pricing and reimbursement strategies, facilitating adoption by dialysis organizations, health care professionals, recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing roxadustat, which would adversely affect our business and financial condition.

Although regulatory approval has been obtained for roxadustat in China, Japan, and Chile, we may be unable to obtain regulatory approval in other countries, or such approval may be delayed or limited, due to a number of factors, many of which are beyond our control.

The clinical trials and the manufacturing of our product candidates are and will continue to be, and the marketing of our product candidates will be, subject to extensive and rigorous review and regulation by numerous government authorities in the United States ("U.S.") and in other countries where we intend to develop and, if approved, market any product candidates. Before obtaining regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical trials and clinical trials that the product candidate is safe and effective for use in each indication for which approval is sought. The regulatory review and approval process is expensive and requires substantial resources and time, and in general, very few product candidates that enter development ultimately receive regulatory approval. In addition, our collaboration partners for roxadustat have final control over development decisions in their respective territories and they may make decisions with respect to development or regulatory authorities that delay or limit the potential approval of roxadustat, or increase the cost of development or commercialization. Accordingly, we may be unable to successfully develop or commercialize roxadustat, pamrevlumab, or any of our other product candidates in one or more indications and jurisdictions.

Moreover, for any Phase 3 clinical trial to support an NDA/Biologics License Application submission for approval, the U.S. Food and Drug Administration ("FDA") and foreign regulatory authorities require compliance with regulations and standards (including good clinical practices ("GCP") requirements for designing, conducting, monitoring, recording, analyzing, and reporting the results of clinical trials) to ensure that (1) the data and results from trials are credible and accurate; and (2) that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we as the sponsor remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our clinical research organizations ("CROs"), trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, the clinical data generated in our clinical trials may be deemed unreliable. Accordingly, the FDA or other regulatory authorities may require us to exclude the use of patient data from these unreliable clinical trials, or perform additional clinical trials before approving our marketing applications. The FDA or other regulatory authorities may even reject our application for approval or refuse to accept our future applications.

Regulatory authorities may take actions or impose requirements that delay, limit or deny approval of our product candidates for many reasons, including, among others:

- our failure to adequately demonstrate to the satisfaction of regulatory authorities that roxadustat is safe and effective in treating anemia in CKD or that pamrevlumab is safe and effective in treating IPF, pancreatic cancer, or DMD;
- our failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- our failure of clinical trials to meet the level of statistical significance required for approval;
- the determination by regulatory authorities that additional clinical trials are necessary to demonstrate the safety and efficacy of roxadustat or pamrevlumab, or that ongoing clinical trials need to be modified in design, size, conduct or implementation;
- our product candidates may exhibit an unacceptable safety signal as they advance through clinical trials, in particular controlled Phase 3 trials;

- the CROs that conduct clinical trials on our behalf may take actions outside of our control that materially adversely impact our clinical trials;
- we or third-party contractors manufacturing our product candidates may not maintain current good manufacturing practices ("cGMP"), successfully pass inspection or meet other applicable manufacturing regulatory requirements;
- regulatory authorities may not agree with our interpretation of the data from our preclinical trials and clinical trials; or
- · collaboration partners may not perform or complete their clinical programs in a timely manner, or at all.

Any of these factors, many of which are beyond our control, could jeopardize our or our collaboration partners' abilities to obtain regulatory approval for our product candidates in one or more indications.

The FDA or other regulatory authorities may require more information (including additional preclinical or clinical data to support approval), which may delay or prevent approval or cause us to abandon the development program altogether. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of Risk Evaluation and Mitigation Strategy ("REMS") (or other regulatory authorities may require the establishment of a similar strategy), that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us.

The results of the FDA Cardiovascular and Renal Drugs Advisory Committee meeting may affect roxadustat's approvability or label in CKD anemia.

On March 1, 2021, the FDA informed us that the Cardiovascular and Renal Drugs Advisory Committee will hold an advisory committee meeting to review the NDA for roxadustat. The date of the advisory committee meeting has not been set. As a result of this communication, we will not receive an approval decision by the PDUFA goal date of March 20, 2021. The advisory committee is a committee of external experts which will provide input on issues relating to benefit, risk, and interpretation of our roxadustat clinical trial data. We do not know when the FDA will convene the advisory committee or how long it will take after the committee convenes for the FDA to make a decision on our NDA. The results of the advisory committee may affect roxadustat's approvability or label. The FDA may further delay approval of our NDA if applicable regulatory criteria are not satisfied and/or the FDA requires additional testing or information. The full extent of the delay on an approval decision and impact of the advisory committee is unknown.

Preclinical, Phase 1 and Phase 2 clinical trial results may not be indicative of the results that may be obtained in larger clinical trials.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical and early clinical trials, which are often highly variable and use small sample sizes, may not be predictive of similar results in humans or in larger, controlled clinical trials, and successful results from clinical trials in one indication may not be replicated in other indications.

Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and we may face similar setbacks.

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We do not know whether our ongoing or planned clinical trials of roxadustat or pamrevlumab will need to be redesigned based on interim results or if we will be able to achieve sufficient patient enrollment or complete planned clinical trials on schedule.

Clinical trials can be delayed or terminated for a variety of reasons, including delay or failure to:

- address any physician or patient safety concerns that arise during the course of the trial;
- obtain required regulatory or institutional review board approval or guidance;
- reach timely agreement on acceptable terms with prospective CROs and clinical trial sites;
- recruit, enroll and retain patients through the completion of the trial, including for the duration of the Severe Acute Respiratory Syndrome Coronavirus 2 and the resulting Coronavirus Disease ("COVID-19") pandemic;
- maintain clinical sites in compliance with clinical trial protocols;
- initiate or add a sufficient number of clinical trial sites; and
- manufacture sufficient quantities of product candidate for use in clinical trials.

In particular, identifying and qualifying patients to participate in clinical trials of our product candidates is critical to our success. The timing of our clinical trials depends on the rate at which we can recruit and enroll patients in testing our product candidates. Patients may be unwilling to participate in clinical trials of our product candidates for a variety of reasons, some of which may be beyond our control, including:

- severity of the disease under investigation;
- availability of alternative treatments;
- size and nature of the patient population;
- eligibility criteria for and design of the study in question;
- perceived risks and benefits of the product candidate under study;
- ability to enroll patients in clinical trials during the COVID-19 pandemic (particularly for IPF);
- ongoing clinical trials of competitive agents;
- physicians' and patients' perceptions of the potential advantages of our product candidates being studied in relation to available therapies or other products under development:
- our CRO's and our trial sites' efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients and collect patient data adequately during and after treatment.

If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials.

In addition, we could encounter delays if a clinical trial is suspended or terminated by us, by the relevant institutional review boards at the sites at which such trials are being conducted, or by the FDA or other regulatory authorities. A suspension or termination of clinical trials may result from any number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, changes in laws or regulations, or a principal investigator's determination that a serious adverse event could be related to our product candidates. Any delays in completing our clinical trials will increase the costs of the trial, delay the product candidate development and approval process and jeopardize our ability to commence marketing and generate revenues. Any of these occurrences may materially and adversely harm our business, operations, and prospects.

Our product candidates may cause or have attributed to them undesirable side effects or have other properties that delay or prevent their regulatory approval or limit their commercial potential.

Undesirable side effects caused by our product candidates or that may be identified as related to our product candidates by physician investigators conducting our clinical trials or even competing products in development that utilize a similar mechanism of action or act through a similar biological disease pathway could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. If we determine that there is a likely causal relationship between a serious adverse event and our product candidate, and such safety event is material or significant enough, it may result in:

- our clinical trial development plan becoming longer and more extensive;
- regulatory authorities increasing the data and information required to approve our product candidates and imposing other requirements; and
- our collaboration partners terminating our existing agreements.

The occurrence of any or all of these events may cause the development of our product candidates to be delayed or terminated, which could materially and adversely affect our business and prospects. Refer to "Business - Overview" in our Annual Report on Form 10-K for the year ended December 31, 2020 for a discussion of the adverse events and serious adverse events that have emerged in clinical trials of roxadustat and pamrevlumab.

Clinical trials of our product candidates may not uncover all possible adverse effects that patients may experience.

Clinical trials are conducted in representative samples of the potential patient population, which may have significant variability. Clinical trials are by design based on a limited number of subjects and of limited duration for exposure to the product used to determine whether, on a potentially statistically significant basis, the planned safety and efficacy of any product candidate can be achieved. As with the results of any statistical sampling, we cannot be sure that all side effects of our product candidates may be uncovered, and it may be the case that only with a significantly larger number of patients exposed to the product candidate for a longer duration, that a more complete safety profile is identified. Further, even larger clinical trials may not identify rare serious adverse effects or the duration of such studies may not be sufficient to identify when those events may occur. There have been other products, including erythropoiesis stimulating agents ("ESAs"), for which safety concerns have been uncovered following approval by regulatory authorities. Such safety concerns have led to labeling changes or withdrawal of ESAs products from the market. While our most advanced product candidate is chemically unique from ESAs, it or any of our product candidates may be subject to known or unknown risks. Patients treated with our products, if approved, may experience adverse reactions and it is possible that the FDA or other regulatory authorities may ask for additional safety data as a condition of, or in connection with, our efforts to obtain approval of our product candidates. If safety problems occur or are identified after our product candidates reach the market, we may, or regulatory authorities may require us to amend the labeling of our products, recall our products or even withdraw approval for our products.

If we or our manufactures cannot properly manufacture sufficient product, we may experience delays in development, regulatory approval, launch or successful commercialization.

Completion of our clinical trials and commercialization of our products require access to, or development of, facilities to manufacture and manage our product candidates at sufficient yields, quality and at commercial scale. Although we have entered into commercial supply agreements for roxadustat and pamrevlumab, we will need to enter into additional commercial supply agreements, including for backup or second source third-party manufacturers. We may not be able to enter into these agreements with satisfactory terms or on a timely manner. In addition, we may experience delays or technical problems associated with technology transfer of manufacturing processes to any new suppliers.

We have limited experience manufacturing or managing third parties in manufacturing any of our product candidates in the volumes that are expected to be necessary to support large-scale clinical trials and sales. In addition, we have limited experience forecasting supply requirements or coordinating supply chain (including export management) for launch or commercialization, which is a complex process involving our third-party manufacturers and logistics providers, and for roxadustat, our collaboration partners. We may not be able to accurately forecast supplies for commercial launch, or do so in a timely manner and our efforts to establish these manufacturing and supply chain management capabilities may not meet our requirements as to quantities, scale-up, yield, cost, potency or quality in compliance with cGMP, particularly if the marketing authorization or market uptake is more rapid than anticipated or we have an unanticipated surge in demand.

We have a limited amount of roxadustat and pamrevlumab in storage, limited capacity reserved at our third-party manufactures, and, even if we have or are able to put supply agreements in place for our products, there are long lead times required to manufacture and scale-up the manufacture of additional supply, as required for both late-stage clinical trials, post-approval trials, and commercial supply. If we are unable to forecast, order or manufacture sufficient quantities of roxadustat or pamrevlumab on a timely basis, it may delay our development, launch or commercialization in some or all indications we are currently pursuing. Any delay or interruption in the supply of our product candidates or products could have a material adverse effect on our business and operations.

Our commercial drug product and the product we use for clinical trials must be produced under applicable cGMP regulations. Failure to comply with these regulations may require us to recall commercial product or repeat clinical trials, which would impact sales revenue or delay the regulatory approval process.

We may add or change manufacturers for our products. We may also make changes to our manufacturing processes or to our product specifications, including in order to accommodate changes in regulations, manufacturing equipment or to account for different processes at new or second source suppliers. If we make any such changes with respect to roxadustat or pamrevlumab we will need to demonstrate comparability to the products and processes already approved or in approval by various regulatory authorities, including potentially through the conduct of additional clinical trials. Even if we do demonstrate comparability, a regulatory agency could challenge that result which could delay our development or commercialization progress. Any of these occurrences may materially impact our operations and potential profitability.

We, and even an experienced third-party manufacturer, may encounter difficulties in production. Difficulties may include:

- costs and challenges associated with scale-up and attaining sufficient manufacturing yields, in particular for biologic products such as pamrevlumab, which is a monoclonal antibody;
- contracting with additional suppliers and validation/qualification of additional facilities to meet growing demand;
- supply chain issues, including coordination of multiple contractors in our supply chain and securing necessary licenses (such as export licenses);
- the timely availability and shelf life requirements of raw materials and supplies;
- limited stability and product shelf life;
- equipment maintenance issues or failure;
- quality control and quality assurance issues;
- shortages of qualified personnel and capital required to manufacture large quantities of product;
- · compliance with regulatory requirements that vary in each country where a product might be sold;
- · capacity or forecasting limitations and scheduling availability in contracted facilities; and
- natural disasters, such as pandemics, including the COVID-19 pandemic, floods, storms, earthquakes, tsunamis, and droughts, or accidents such as fire, that affect facilities, possibly limit or postpone production, and increase costs.

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Regulatory authorities will do their own benefit risk analysis and may reach a different conclusion than we or our partners have, and these regulatory authorities may base their approval decision on different analyses, data, and statistical methods than ours.

Even if we believe we have achieved positive clinical results, such as superiority or non-inferiority, in certain endpoints, populations or subpopulations, or using certain statistical methods of analysis, the FDA and European Medicines Agency ("EMA") will each conduct their own benefit-risk analysis and may reach different conclusions, using different statistical methods, different endpoints or definitions thereof, or different patient populations or sub-populations, and regulatory authorities may change their approvability criteria based on their internal analyses and discussions with expert advisors. Regulatory authorities may approve roxadustat for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-approval clinical trials. While we will present to regulatory authorities certain pre-specified and not pre-specified sub-populations and sub-group analyses (for example, incident dialysis), multiple secondary endpoints, and multiple analytical methods (such as long-term follow up analyses), including adjusted and censored data, regulatory authorities may reject these analyses, methods, or even parts of our trial design or certain data from our studies, the rationale for our pre-specified non-inferiority margins or other portions of our statistical analysis plans. In addition, even if we are able to provide positive data with respect to certain analyses, such as incident dialysis, estimated glomerular filtration rate, hepcidin, or quality of life measures, regulatory authorities may not include such claims on any approved labeling for roxadustat, which may limit the commercialization or market opportunity for roxadustat. The failure to obtain regulatory approval, or any label, population or other approval limitations in any jurisdiction, may significantly limit our ability to generate revenues, and any failure to obtain such approval for all of the indications and labeling claims we deem desirable could reduce our potential revenue.

Even if we are able to obtain regulatory approval of our product candidates, the label we obtain may limit the indicated uses for which our product candidates may be marketed.

With respect to roxadustat, regulatory approvals obtained, could limit the approved indicated uses for which roxadustat may be marketed. For example, our label approved in Japan, includes the following warning: "Serious thromboembolism such as cerebral infarction, myocardial infarction, and pulmonary embolism may occur, possibly resulting in death, during treatment with roxadustat." Additionally, in the U.S., ESAs have been subject to significant safety warnings, including the boxed warnings on their labels. The safety concerns relating to ESAs may result in labeling for roxadustat containing similar warnings even if our Phase 3 clinical trials do not suggest that roxadustat has similar safety issues. Even if the label for roxadustat does not contain all of the warnings contained in the boxed warning for ESAs, the label for roxadustat may contain other warnings or limit the market opportunity or approved indications for roxadustat. These warnings could include warnings against exceeding specified hemoglobin targets and other warnings that derive from the lack of clarity regarding the safety issues associated with ESAs, even if our Phase 3 clinical trials do not themselves raise safety concerns.

We face substantial competition in the discovery, development and commercialization of product candidates.

The development and commercialization of new pharmaceutical products is highly competitive. Our future success depends on our ability and/or the ability of our collaboration partners to achieve and maintain a competitive advantage with respect to the development and commercialization of our product candidates. Our objective is to discover, develop and commercialize new products with superior efficacy, convenience, tolerability, and safety. We expect that in many cases, the products that we commercialize will compete with existing, market-leading products of companies that have large, established commercial organizations.

If roxadustat is approved and launched commercially, competing drugs are expected to include ESAs, particularly in those patient segments where ESAs are used. Currently available ESAs include epoetin alfa (EPOGEN®, marketed by Amgen Inc. in the U.S., Procrit® and Erypo®/Eprex®, marketed by Johnson & Johnson Inc., and Espo® marketed by Kyowa Hakko Kirin in Japan and China), darbepoetin (Amgen/Kyowa Hakko Kirin's Aranesp® and NESP®) and Mircera® marketed by Hoffmann-La Roche ("Roche") outside of the U.S. and by Vifor Pharma, a Roche licensee, in the U.S. and Puerto Rico, as well as biosimilar versions of these currently marketed ESA products. ESAs have been used in the treatment of anemia in CKD for more than 30 years, serving a significant majority of dialysis CKD patients. While non-dialysis CKD patients who are not under the care of nephrologists, including those with diabetes and hypertension, do not typically receive ESAs and are often left untreated, some non-dialysis patients under nephrology or hematology care may be receiving ESA therapy. It may be difficult to encourage healthcare providers and patients to switch to roxadustat from products with which they have become familiar.

We may also face competition from potential new anemia therapies currently in clinical development, including in those patient segments not adequately addressed by ESAs. Companies that are currently developing hypoxia-inducible factor ("HIF") prolyl hydroxylase (together with HIF, "HIF-PH") inhibitors for anemia in CKD indications include GlaxoSmithKline plc ("GSK"), Bayer Corporation ("Bayer"), Akebia Therapeutics, Inc. ("Akebia"), Otsuka Pharmaceutical ("Otsuka"), Akebia's partner in the U.S. and Europe, Japan Tobacco, and Zydus Cadila (India) ("Zydus"). Akebia has completed Phase 3 studies in CKD patients on dialysis and not on dialysis in the U.S., as well as a Phase 3b, randomized, open-label, active-controlled trial evaluating the efficacy and safety of oral vadadustat once daily and three times weekly for the maintenance treatment of anemia in hemodialysis subjects converting from erythropoiesis stimulating agents. The study completion date is estimated to be May 2022. Akebia announced an additional Phase 3 study evaluating the efficacy and safety of dose conversion from a long-acting erythropoiesis stimulating agent (Mircera®) to three times weekly oral vadadustat for the maintenance treatment of anemia in hemodialysis subjects. The estimated study start date is February 2021. Akebia has publicly stated their intent to file the vadadustat NDA in the U.S. in the second quarter of 2021.

In Japan, Mitsubishi Tanabe Pharmaceutical Corporation, Akebia's collaboration partner, received approval for vadadustat on June 29, 2020 for the treatment of anemia of CKD patients on and not on dialysis. GSK received approval for daprodustat in Japan on June 29, 2020 for the treatment of anemia of CKD patients on and not on dialysis. Price listing for the launch in Japan of both vadadustat and daprodustat occurred in the third quarter of 2020, with pricing in line with roxadustat pricing. GSK is also conducting global Phase 3 studies in CKD patients on dialysis and not on dialysis, and expects to complete those studies by March 2022. GSK and Kyowa Hakko Kirin announced in November 2018 that the two companies signed a strategic commercialization deal in Japan for daprodustat. Bayer has completed global Phase 2 studies and its HIF-PH inhibitor is now in Phase 3 development in CKD populations on dialysis and not on dialysis in Japan. Japan Tobacco received approval in Japan for enarodustat for the treatment of anemia in CKD patients on dialysis and not on dialysis, to be sold by Torii Pharmaceuticals Ltd as ENAROY®. Japan Tobacco and its partner JW Pharmaceuticals started a Phase 3 study in dialysis patients in Korea in 2019. Zydus started Phase 3 studies in dialysis and non-dialysis CKD patients in India in 2019.

In July 2020, Zydus received approval from the FDA to begin a Phase 1 study of desidustat for the treatment of chemotherapy-induced anemia, which could potentially be competitive with roxadustat within this indication.

Reblozyl® (luspatercept) was approved by the FDA in April 2020 for the treatment of anemia in adults with myelodysplastic syndromes with ring sideroblasts or myelodysplastic/myeloproliferative neoplasms with ring sideroblasts and thrombocytosis who need regular red blood cell transfusions and have not responded well to or cannot receive an ESA. It is the first and only erythroid maturation agent approved in the U.S., Europe, and Canada and is part of a global collaboration between Acceleron Pharma, Inc. and Bristol Myers Squibb. In 2020, Reblozyl net revenue was \$274 million, including \$115 million in Q4 2020.

In addition, we will likely face competition from other companies developing biologic therapies for the treatment of other anemia indications that we may also seek to pursue in the future. We may face competition for patient recruitment, enrollment for clinical trials, and potentially in commercial sales. There may also be new therapies for renal-related diseases that could limit the market or level of reimbursement available for roxadustat.

In China, ESA is considered the standard of care for treatment of anemia of CKD, and locally manufactured epoetin alfa is offered by 15 local manufacturers including the market leader EPIAO that is marketed by 3SBio Inc. We may face potential competition from other HIF-PH inhibitors. Companies active in the US such as Akebia, Bayer, and GSK have been authorized by the National Medical Products Administration ("NMPA") to conduct trials in China to support its ex-China regulatory filings. A number of domestic companies, including Jiangsu Hengrui Medicine Co., Ltd., Guandong Sunshine Health Investment Co., Ltd., 3SBio Inc., and Hangzhou Andao Pharmaceutical Co. have been permitted by the NMPA to conduct clinical trials in their locally-developed HIF-PH inhibitor investigational compounds for the treatment of anemia in CKD. Domestic companies are also in-licensing global compounds to be developed as domestic drugs, including China Medical System which in-licensed desidustat, a compound that is currently in Phase 3 trials in India, from Zydus for greater China in January 2020. In January 2021, China Medical System Holdings Ltd. was granted approval by the Chinese NMPA to begin trials for desidustat in patients with anemia of CKD, including dialysis and non-dialysis patients. Shenzhen Salubris Pharmaceutical Co., Ltd., a domestic company in China, has in-licensed enarodustat from Japan Tobacco and received NMPA approval in the third quarter of 2020 to initiate Phase 3 studies. We will also face competition from generics who could enter the market after expiry of our patents in China, and two potential market players have already started bioequivalence studies, including Chia Tai-Tiangqing Pharmaceutical Holdings and CSPA Pharmaceutical Group.

The first biosimilar ESA, Pfizer's Retacrit® (epoetin zeta), entered the U.S. market in November 2018. Market penetration of Retacrit and the potential addition of other biosimilar ESAs currently under development may alter the competitive and pricing landscape of anemia therapy in CKD patients on dialysis under the end-stage renal disease bundle. The patents for Amgen's EPOGEN® (epoetin alfa) expired in 2004 in Europe, and the final material patents in the U.S. expired in May 2015. Several biosimilar versions of currently marketed ESAs are available for sale in Europe, China and other territories. In the U.S., a few ESA biosimilars are currently under development. Sandoz, a division of Novartis, markets Binocrit® (epoetin alfa) in Europe and may file a biosimilar Biologics License Application in the U.S.

The majority of the current CKD anemia market focuses on dialysis patients, who visit dialysis centers on a regular basis, typically three times a week, and anemia therapies are administered as part of the visit. Two of the largest operators of dialysis clinics in the U.S., DaVita Healthcare Partners Inc. ("DaVita"), and Fresenius Medical Care AG & Co. KGaA ("Fresenius"), collectively provide dialysis care to more than 80% of U.S. dialysis patients, and therefore have historically executed long-term contracts including rebate terms with Amgen. Successful penetration in this market will likely require our partner AstraZeneca to enter into a definitive agreement with Fresenius, DaVita, or other dialysis organizations, on favorable pricing terms and on a timely basis.

If approved and launched commercially to treat IPF, pamrevlumab is expected to compete with Roche's Esbriet® (pirfenidone), and Boehringer Ingelheim's Ofev® (nintedanib). We believe that if pamrevlumab can be shown to safely stabilize or reverse lung fibrosis, and thus stabilize or improve lung function in IPF patients, it can compete with pirfenidone and nintedanib for market share in IPF. However, it may be difficult to encourage treatment providers and patients to switch to pamrevlumab from an oral product with which they are already familiar to a product delivered via in-office infusion. Furthermore, pirfenidone and nintedanib may be produced as generics in the near future. We may also face competition from potential new IPF therapies in recruitment and enrollment in our clinical trials and potentially in commercialization.

Pamrevlumab is a monoclonal antibody that may be more expensive and less convenient than oral small molecules such as nintedanib and pirfenidone. Other potential competitive product candidates in various stages of development for IPF include Kadmon Holdings, Inc.'s KD025, Liminal BioSciences' PBI-4050, and Roche/Promedior, Inc.'s PRM-151.

If pamrevlumab is approved and launched commercially to treat locally advanced pancreatic cancer patients who are not candidates for surgical resection, pamrevlumab may face competition from products currently used for pancreatic cancer. These include FOLFRINOX, a combination chemotherapy regimen of folic acid, 5-fluouracil, oxaliplatin and irinotecan, and agents seeking approval in combination with gemcitibine and nab-paclitaxel from companies such as Rafael Pharma's defactinib/CPI-613 and Merrimack's istiratumab. Gemcitabine and/or nab-paclitaxel are the current standard of care in the first-line treatment of metastatic pancreatic cancer.

Celgene Corporation's Abraxane® (nab-paclitaxel) was launched in the U.S. and Europe in 2013 and 2014, and was the first drug approved in this disease in nearly a decade.

If approved and launched commercially to treat DMD, pamrevlumab is expected to face competition from drugs that have been approved in major markets such as the U.S., European Union, and Japan. On September 19, 2016, the FDA approved Sarepta Therapeutics Inc.'s ("Sarepta") Exondys 51TM (eteplirsen). Exondys 51 is approved to treat patients who have a mutation of the dystrophin gene amenable to exon 51 skipping, representing approximately 13% of patients with DMD. In Europe, Sarepta received a negative opinion for its marketing application for eteplirsen from the EMA in September 2018. Sarepta has reported a full year Exondys 51 revenue of \$380 million in 2019. Sarepta's Vyondys 53TM (golodirsen) was approved by the FDA in December 2019 for patients with a confirmed genetic mutation that is amenable to exon 53 skipping, which accounts for approximately 8% of the DMD population. Sarepta's Amondys 45TM (casimersen) was approved by the FDA in February 2021 for patients with a confirmed genetic mutation that is amenable to exon 45 skipping, which accounts for approximately 8% of the DMD population.

PTC Therapeutics' product Translarna TM received a conditional approval in Europe in 2014, which was renewed in November 2016 with a request for a new randomized placebo-controlled 18-month study by the Committee for Medicinal Products for Human Use of the EMA; however, the FDA informed the sponsor in a complete response letter in October 2017, as well as in its response to PTC Therapeutics' appeal, that the FDA is unable to approve the application in its current form. An additional Phase 3 study is currently ongoing. While Translarna TM targets a different set of DMD patients from those targeted by Sarepta's Exondys 51®, it is also limited to a subset of patients who carry a specific mutation. Conversely, pamrevlumab is intended to treat DMD patients without limitation to type of mutation.

Pamrevlumab may also face competition from other drugs currently in clinical development in patient recruiting and enrollment in clinical trials, and, if approved, in commercialization. Examples of those compounds currently under clinical development are the drug candidates from Pfizer, Pliant, Galecto, and Sarepta. Pfizer initiated a Phase 3 study with PF-06939926, its AAV9 mini-dystrophin gene therapy for DMD in February 2020. Pliant's PLN-74809 and Galecto's lead candidate GB0139, are in Phase 2 development for IPF.

The success of any or all of these potential competitive products may negatively impact the development and potential for success of pamrevlumab. In addition, any competitive products that are on the market or in development may compete with pamrevlumab for patient recruitment and enrollment for clinical trials or may force us to change our clinical trial design, including, in order to compare pamrevlumab against another drug, which may be the new standard of care.

Moreover, many of our competitors have significantly greater resources than we do. Large pharmaceutical companies, in particular, have extensive experience in clinical testing, obtaining regulatory approvals, recruiting patients, manufacturing pharmaceutical products, and commercialization. In the potential anemia market for roxadustat, for example, large and established companies such as Amgen and Roche, among others, compete aggressively to maintain their market shares. In particular, the currently marketed ESA products are supported by large pharmaceutical companies that have greater experience and expertise in commercialization in the anemia market, including in securing reimbursement, government contracts and relationships with key opinion leaders; conducting testing and clinical trials; obtaining and maintaining regulatory approvals and distribution relationships to market products; and marketing approved products. These companies also have significantly greater scale, research and marketing capabilities than we do and may also have products that have been approved or are in later stages of development and have collaboration agreements in our target markets with leading dialysis companies and research institutions. If we and our collaboration partners are not able to compete effectively against existing and potential competitors, our business and financial condition may be materially and adversely affected.

No or limited reimbursement or insurance coverage of our approved products, if any, by third-party payors may render our products less attractive to patients and healthcare providers.

Market acceptance and sales of any approved products will depend significantly on reimbursement or coverage of our products by government or third-party payors and may be affected by existing and future healthcare reform measures or prices of related products for which the government or third-party reimbursement applies. Coverage and reimbursement by the government or a third-party payor may depend upon a number of factors, including the payor's determination that use of a product is:

- a covered benefit under applicable health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- · cost-effective; and
- · neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product from a government or other third-party payor is a time consuming and costly process that could require us to provide supporting scientific, clinical and cost-effectiveness data for the use of our products to the payor, which we may not be able to provide. Furthermore, the reimbursement policies of governments and third-party payors may significantly change in a manner that renders our clinical data insufficient for adequate reimbursement or otherwise limits the successful marketing of our products. Even if we obtain coverage for our product candidates, the pricing may be subject to re-negotiations or third-party payors may not establish adequate reimbursement amounts, which may reduce the demand for, or the price of, our products. For example, our current National Reimbursement Drug List reimbursement pricing for China is effective for a standard two-year period (between January 1, 2020 to December 31, 2021), after which time we will have to renegotiate a new price for roxadustat, which we expect to be lower based upon historical precedents.

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Reference pricing is used by various Europe member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, our partner or we may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our product candidates to other available products in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unacceptable levels, we or our partner may elect not to commercialize our products in such countries, and our business and financial condition could be adversely affected.

Risks Related to Severe Acute Respiratory Syndrome Coronavirus 2 and the Resulting Coronavirus Disease ("COVID-19")

Our business could continue to be adversely affected by the ongoing COVID-19 global pandemic.

The effects of the COVID-19 pandemic, the associated government-mandated restrictions and the other effects on healthcare systems, the economy, and society as a whole, may negatively impact productivity, disrupt our business, and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the progression of the disease, the length and severity of the restrictions, and other impacts and limitations on our ability to conduct our business in the ordinary course. These disruptions in our operations could negatively impact our business, operating results, and financial condition. While certain COVID-19 vaccines have received regulatory approval, it is uncertain if and when sufficient vaccines will have been distributed to lessen the economic and other effects of COVID-19, and the efficacy of such vaccines in preventing the spread and effects of COVID-19 and other variants is unclear.

The extent of the impact on the COVID-19 pandemic on our business and financial results will continue to depend on numerous evolving factors that we are not able to accurately predict and which will vary by market, including the duration and scope of the pandemic, global economic conditions during and after the pandemic, the speed and efficacy of vaccinations around the world, and governmental actions that have been taken, or may be taken in the future, in response to the pandemic.

We have taken measures to minimize the health risks of COVID-19 to our staff, patients, healthcare providers, and their communities, as their safety and well-being are our top priority. Despite these efforts, there is a risk that one or more of our employees, including members of senior management, could contract COVID-19. Our U.S. employees are working remotely when possible, and we may experience reduced productivity due to the remote work environment. In addition, there are other risks from remote work including but not limited to the potential for reduced oversight of third parties we work with, such as manufacturing and clinical sites.

China was able to minimize the impact of COVID-19 on the economy in 2020 relative to other major economies. However, if there are any further COVID-19 outbreaks, we or our partners may need to re-institute or tighten restrictions on our operations.

We have seen impacts from COVID-19 on all of our clinical trials to varying degrees. There is a risk that any or all of our clinical trials will be further delayed, in particular our studies in IPF, due to a continued or further outbreak which can slow or pause enrollment or site initiation and other direct COVID-19 impacts to clinical sites and clinical service providers. In addition, while we are trying to mitigate the effect of COVID-19 on existing patients, it is possible that some patients may not be able to continue to comply with protocols, which could further delay our clinical trial progress.

We believe we have sufficient roxadustat and pamrevlumab supplies for our expected commercial and clinical requirements over the next year and we and our manufacturing partners are currently continuing manufacturing operations. However, we only have a limited stockpile of these drug supply products, and therefore, if there is a greater impact from the COVID-19 pandemic than we have expected, or if manufacturing operations are halted again, or if drug product expires due to slowed clinical trials, we could face shortages in our global supply chains. COVID-19 has created increased demand for the limited global biologics manufacturing capacity, and as a result, we have faced competition for manufacturing supplies due to prioritization of COVID-19 related manufacturing. We could face additional competition for such manufacturing supplies, including reagents, supplements and media, and may face competition to use available capacity at our manufacturing partners. Any such supply disruptions could adversely impact our clinical development and ability to generate revenues from our approved products and our business, financial condition, results of operations and growth prospects could be materially adversely affected. There may be unexpected regulatory delays due to the COVID-19 pandemic including due to travel restrictions impacting pre-approval inspections.

Due to these and potentially additional business disruptions, there may be delays to any of our business areas including our drug supply chains, problems with our distribution or warehousing vendors, or delays to our (and our partners') clinical trials or other development efforts, or commercialization and launch activities. The full extent of these effects are unknown, but all of them could have a material impact on our operations and revenue.

In addition, to the extent the ongoing COVID-19 pandemic adversely affects our business and results of operations, it may also have the effect of heightening many of the other risks and uncertainties described in this "Risk Factors" section.

Risks Related to Our Reliance on Third Parties

If our collaborations were terminated or if Astellas or AstraZeneca were to prioritize other initiatives over their collaborations with us, our ability to successfully develop and commercialize our product candidates would suffer.

We have entered into collaboration agreements with respect to the development and commercialization of our lead product candidate, roxadustat, with Astellas and AstraZeneca. These agreements provide for reimbursement of our development costs by our collaboration partners and also provide for commercialization of roxadustat throughout the major territories of the world.

Our agreements with Astellas and AstraZeneca provide each of them with the right to terminate their respective agreements with us, upon the occurrence of negative clinical results, delays in the development and commercialization of our product candidates or adverse regulatory requirements or guidance. In addition, each of those agreements provides our respective partners the right to terminate any of those agreements upon written notice for convenience. The termination of any of our collaboration agreements would require us to fund and perform the further development and commercialization of roxadustat in the affected territory, or pursue another collaboration, which we may be unable to do, either of which could have an adverse effect on our business and operations. Moreover, if Astellas or AstraZeneca, or any successor entity, were to determine that their collaborations with us are no longer a strategic priority, or if either of them or a successor were to reduce their level of commitment to their collaborations with us, our ability to develop and commercialize roxadustat could suffer. In addition, our collaborations are exclusive and preclude us from entering into additional collaboration agreements with other parties in the area or field of exclusivity.

If we do not establish and maintain strategic collaborations related to our product candidates, we will bear all of the risk and costs related to the development and commercialization of any such product candidate, and we may need to seek additional financing, hire additional employees and otherwise develop expertise at significant cost. This in turn may negatively affect the development of our other product candidates as we direct resources to our most advanced product candidates.

Our collaboration partners also have certain rights to control decisions regarding the development and commercialization of our product candidates with respect to which they are providing funding. If we have a disagreement over strategy and activities with our collaboration partners, our plans for obtaining regulatory approval may be revised and negatively affect the anticipated timing and potential for success of our product candidates. Even if a product under a collaboration agreement receives regulatory approval, we will remain substantially dependent on the commercialization strategy and efforts of our collaboration partners, and, our collaboration partners have limited or no experience in commercialization of an anemia drug. If our collaboration partners are unsuccessful in their commercialization efforts, our results will be negatively affected.

With respect to our collaboration agreements for roxadustat, there are additional complexities in that our collaboration partners, Astellas and AstraZeneca, and we must reach consensus on our development programs and regulatory activities, including for the NDA in the U.S. and the Marketing Authorization Application in Europe. In addition, there are aspects of commercial operations that require cooperation among the collaboration partners, including safety data reporting. Multi-party decision-making is complex and involves significant time and effort, and there can be no assurance that the parties will cooperate or reach consensus, or that one or both of our partners will not ask to proceed independently in some or all of their respective territories or functional areas of responsibility in which the applicable collaboration partner would otherwise be obligated to cooperate with us. Any disputes or lack of cooperation with us by either Astellas or AstraZeneca, or both, may negatively impact the timing or success of our regulatory approval applications.

We intend to conduct proprietary research programs in specific disease areas that are not covered by our collaboration agreements. Our pursuit of such opportunities could, however, result in conflicts with our collaboration partners in the event that any of our collaboration partners takes the position that our internal activities overlap with those areas that are exclusive to our collaboration agreements. Moreover, disagreements with our collaboration partners could develop over rights to our intellectual property, including the enforcement of those rights. In addition, our collaboration agreements may have provisions that give rise to disputes regarding the rights and obligations of the parties. Any conflict with our collaboration partners could lead to the termination of our collaboration agreements, delay collaborative activities, reduce our ability to renew agreements or obtain future collaboration agreements or result in litigation or arbitration and would negatively impact our relationship with existing collaboration partners, and could impact our commercial results.

Certain of our collaboration partners could also become our competitors in the future. If our collaboration partners develop competing products, fail to obtain necessary regulatory approvals, terminate their agreements with us prematurely or fail to devote sufficient resources to the development and commercialization of our product candidates, the development and commercialization of our product candidates and products could be delayed.

If our preclinical and clinical trial contractors do not properly perform their agreed upon obligations, we may not be able to obtain or may be delayed in receiving regulatory approvals for our product candidates.

We rely heavily on university, hospital, dialysis centers and other institutions and third parties, including the principal investigators and their staff, to carry out our clinical trials in accordance with our clinical protocols and designs. We also rely on a number of third-party CROs to assist in undertaking, managing, monitoring and executing our ongoing clinical trials, including those for roxadustat. We expect to continue to rely on CROs, clinical data management organizations, medical institutions and clinical investigators to conduct our development efforts in the future, including our continued development of roxadustat. We compete with many other companies for the resources of these third parties, and large pharmaceutical companies often have significantly more extensive agreements and relationships with such third-party providers, and such third-party providers may prioritize the requirements of such large pharmaceutical companies over ours. The third parties on whom we rely may terminate their engagements with us at any time, which may cause delay in the development and commercialization of our product candidates. If any such third party terminates its engagement with us or fails to perform as agreed, we may be required to enter into alternative arrangements, which would result in significant cost and delay to our product development program. Moreover, our agreements with such third parties generally do not provide assurances regarding employee turnover and availability, which may cause interruptions in the research on our product candidates by such third parties.

Moreover, while our reliance on these third parties for certain development and management activities will reduce our control over these activities, it will not relieve us of our responsibilities. For example, the FDA and foreign regulatory authorities require compliance with regulations and standards, including GCP requirements for designing, conducting, monitoring, recording, analyzing and reporting the results of clinical trials to ensure that the data and results from trials are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Although we rely on third parties to conduct our clinical trials, we, as the sponsor, remain responsible for ensuring that each of these clinical trials is conducted in accordance with its general investigational plan and protocol under legal and regulatory requirements, including GCP. Regulatory authorities enforce these GCP requirements through periodic inspections of trial sponsors, principal investigators and trial sites.

If any of our CROs, trial sites, principal investigators or other third parties fail to comply with applicable GCP requirements, other regulations, trial protocol or other requirements under their agreements with us, the quality or accuracy of the data they obtain may be compromised or unreliable, and the trials of our product candidates may not meet regulatory requirements. If trials do not meet regulatory requirements or if these third parties need to be replaced, the development of our product candidates may be delayed, suspended or terminated, regulatory authorities may require us to exclude the use of patient data from our approval applications or perform additional clinical trials before approving our marketing applications. Regulatory authorities may even reject our application for approval or refuse to accept our future applications for an extended period of time. We cannot assure that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials comply with GCP requirements or that our results may be used in support of our regulatory submissions. If any of these events occur, we may not be able to obtain regulatory approval for our product candidates on a timely basis, at a reasonable cost, or at all.

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We currently rely, and expect to continue to rely, on third parties to conduct many aspects of our product manufacturing and distribution, and these third parties may terminate these agreements or not perform satisfactorily.

We do not have operating manufacturing facilities at this time other than our roxadustat manufacturing facilities in China, and our current commercial manufacturing plans in China are not expected to satisfy the requirements necessary to support development and commercialization outside of China. Other than in and for China specifically, we do not expect to independently manufacture our products. We currently rely, and expect to continue to rely, on third parties to scale-up, manufacture and supply roxadustat and our other product candidates outside of China. We rely on third parties for distribution, including our collaboration partners and their vendors, except in China where we have established a jointly owned entity with AstraZeneca to manage most of the distribution in China. Risks arising from our reliance on third-party manufacturers include:

- reduced control and additional burdens of oversight as a result of using third-party manufacturers and distributors for all aspects of
 manufacturing activities, including regulatory compliance and quality control and quality assurance;
- termination of manufacturing agreements, termination fees associated with such termination, or nonrenewal of manufacturing agreements with third parties may negatively impact our planned development and commercialization activities;
- the possible misappropriation of our proprietary technology, including our trade secrets and know-how; and
- disruptions to the operations of our third-party manufacturers, distributors or suppliers unrelated to our product, including the merger, acquisition, or bankruptcy of a manufacturer or supplier or a catastrophic event, including disruption resulting from the COVID-19 pandemic, affecting our manufacturers, distributors or suppliers.

Any of these events could lead to development delays or failure to obtain regulatory approval or affect our ability to successfully commercialize our product candidates. Some of these events could be the basis for action by the FDA or another regulatory authority, including injunction, recall, seizure or total or partial suspension of production.

The facilities used by our contract manufacturer to manufacture our product candidates must pass inspections by the FDA and other regulatory authorities. Although, except for China, we do not control the manufacturing operations of, and expect to remain completely dependent on, our contract manufacturers for manufacture of drug substance and finished drug product, we are ultimately responsible for ensuring that our product candidates are manufactured in compliance with cGMP requirements. If our contract manufacturers cannot successfully manufacture material that conforms to our or our collaboration partners' specifications, or the regulatory requirements of the FDA or other regulatory authorities, we may not be able to secure and/or maintain regulatory approval for our product candidates and our development or commercialization plans may be delayed. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. In addition, although our longer-term agreements are expected to provide for requirements to meet our quantity and quality requirements to manufacture our products candidates for clinical studies and commercial sale, we will have minimal direct control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel and we expect to rely on our audit rights to ensure that those qualifications are maintained to meet our requirements. If our contract manufacturers' facilities do not pass inspection by regulatory authorities, or if regulatory authorities do not approve these facilities for the manufacture of our products, or withdraw any such approval in the future, we would need to identify and qualify alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our products, if approved. Moreover, any failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us or adverse regulatory consequences, including clinical holds, warnings or untitled letters, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which would be expected to significantly and adversely affect supplies of our products to us and our collaboration partners.

We have entered into a commercial supply agreement for the manufacture of pamrevlumab with Samsung Biologics Co., Ltd. However, we may experience delays or technical problems associated with technology transfer of the manufacturing process to Samsung and the qualification and scale-up thereof. We have made certain manufacturing commitments to Samsung Biologics Co., Ltd., and there is a risk we will not require the quantities of pamrevlumab we have committed to, particularly if we cease some of our pamrevlumab clinical trials. In addition, our product candidates and any products that we may develop may compete with other product candidates and products for access and prioritization to manufacture. Certain third-party manufacturers may be contractually prohibited from manufacturing our product due to non-compete agreements with our competitors or a commitment to grant another party priority relative to our products. There are a limited number of third-party manufacturers that operate under cGMP and that might be capable of manufacturing to meet our requirements. Due to the limited number of third-party manufacturers with the contractual freedom, expertise, required regulatory approvals and facilities to manufacture our products on a commercial scale, identifying and qualifying a replacement third-party manufacturer would be expensive and time-consuming and may cause delay or interruptions in the production of our product candidates or products, which in turn may delay, prevent or impair our development and commercialization efforts.

We have a letter agreement with IRIX Pharmaceuticals, Inc. ("IRIX"), a third-party manufacturer that we have used in the past, pursuant to which we agreed to negotiate a single source manufacturing agreement that included a right of first negotiation for the cGMP manufacture of HIF-PH inhibitors, including roxadustat, provided that IRIX is able to match any third-party bids within 5%. The exclusive right to manufacture extends for five years after approval of an NDA for those compounds, and any agreement would provide that no minimum amounts would be specified until appropriate by forecast and that we and a commercialization partner would have the rights to contract with independent third parties that exceed IRIX's internal manufacturing capabilities or in the event that we or our commercialization partner determines for reasons of continuity of supply and security that such a need exists, provided that IRIX would supply no less than 65% of the product if it is able to provide this level of supply. Subsequent to the letter agreement, we and IRIX have entered into several additional service agreements. IRIX has requested in writing that we honor the letter agreement with respect to the single source manufacturing agreement, and if we were to enter into any such exclusive manufacturing agreement, there can be no assurance that IRIX will not assert a claim for right to manufacture roxadustat or that IRIX could manufacture roxadustat successfully and in accordance with applicable regulations for a commercial product and the specifications of our collaboration partners. In 2015, Patheon Pharmaceuticals Inc., a business unit of DPx Holdings B.V., acquired IRIX, and in 2017, ThermoFisher Scientific Inc. acquired Patheon Pharmaceuticals Inc.

If any third-party manufacturer terminates its engagement with us or fails to perform as agreed, we may be required to find replacement manufacturers, which would result in significant cost and delay to our development programs. Although we believe that there are several potential alternative manufacturers who could manufacture our product candidates, we may incur significant delays and added costs in identifying, qualifying and contracting with any such third party or potential second source manufacturer. In any event, with any third-party manufacturer we expect to enter into technical transfer agreements and share our know-how with the third-party manufacturer, which can be time-consuming and may result in delays. These delays could result in a suspension or delay of marketing roxadustat.

Certain components of our products are acquired from single-source suppliers or without long-term supply agreements. The loss of these suppliers, or their failure to supply, would materially and adversely affect our business.

We do not have an alternative supplier of certain components of our product candidates. We may be unable to enter into long-term commercial supply arrangements for some of our products, or do so on commercially reasonable terms, which could have a material adverse impact upon our business. In addition, we currently rely on our contract manufacturers to purchase from third-party suppliers some of the materials necessary to produce our product candidates. We do not have direct control over the acquisition of those materials by our contract manufacturers.

The logistics of our supply chain, which include shipment of materials and intermediates from countries such as China and India add additional time and risk (including risk of loss) to the manufacture of our product candidates. While we have in the past maintained sufficient inventory of materials, active pharmaceutical ingredients ("API"), and drug product to meet our and our collaboration partners' needs for roxadustat to date, the lead-time and regulatory approvals required to source from and into countries outside of the U.S. increase the risk of delay and potential shortages of supply.

Risks Related to Our Intellectual Property

If our efforts to protect our proprietary technologies are not adequate, we may not be able to compete effectively in our market.

We rely upon a combination of patents, trade secret protection, and contractual arrangements to protect the intellectual property related to our technologies. We will only be able to protect our products and proprietary information and technology by preventing unauthorized use by third parties to the extent that our patents, trade secrets, and contractual position allow us to do so. Any disclosure to or misappropriation by third parties of our trade secrets or confidential information could compromise our competitive position. Moreover, we are involved in, have in the past been involved in, and may in the future be involved in legal proceedings involving our intellectual property initiated by third parties, which proceedings can be associated with significant costs and commitment of management time and attention. As our product candidates continue in development, third parties have attempted and may again attempt to challenge the validity and enforceability of our patents and proprietary information and technologies.

We also are involved in, have in the past been involved in, and may in the future be involved in initiating legal or administrative proceedings involving the product candidates and intellectual property of our competitors. These proceedings can result in significant costs and commitment of management time and attention, and there can be no assurance that our efforts would be successful in preventing or limiting the ability of our competitors to market competing products.

Composition-of-matter patents relating to the API are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection not limited to any one method of use. Method-of-use patents protect the use of a product for the specified method(s), and do not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. We rely on a combination of these and other types of patents to protect our product candidates, and there can be no assurance that our intellectual property will create and sustain the competitive position of our product candidates.

Biotechnology and pharmaceutical product patents involve highly complex legal and scientific questions and can be uncertain. Any patent applications that we own or license may fail to result in issued patents. Even if patents do successfully issue from our applications, third parties may challenge their validity or enforceability, which may result in such patents being narrowed, invalidated, or held unenforceable. Even if our patents and patent applications are not challenged by third parties, those patents and patent applications may not prevent others from designing around our claims and may not otherwise adequately protect our product candidates. If the breadth or strength of protection provided by the patents and patent applications we hold with respect to our product candidates is threatened, competitors with significantly greater resources could threaten our ability to commercialize our product candidates. Discoveries are generally published in the scientific literature well after their actual development, and patent applications in the U.S. and other countries are typically not published until 18 months after their filing, and in some cases are never published. Therefore, we cannot be certain that we or our licensors were the first to make the inventions claimed in our owned and licensed patents or patent applications, or that we or our licensors were the first to file for patent protection covering such inventions. Subject to meeting other requirements for patentability, for U.S. patent applications filed prior to March 16, 2013, the first to invent the claimed invention is entitled to receive patent protection for that invention while, outside the U.S., the first to file a patent application encompassing the invention is entitled to patent protection for the invention. The U.S. moved to a "first to file" system under the Leahy-Smith America Invents Act, effective March 16, 2013. This system also includes procedures for challenging issued patents and pending patent applications, which creates additional uncertainty. We have, are, and may again become involved in opposition or interference proceedings challenging our patents and patent applications or the patents and patent applications of others, and the outcome of any such proceedings are highly uncertain. An unfavorable outcome in any such proceedings could reduce the scope of or invalidate our patent rights, allow third parties to commercialize our technology and compete directly with us, or result in our inability to manufacture, develop or commercialize our product candidates without infringing the patent rights of others.

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In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how, information, or technology that is not covered by our patents. Although our agreements require all of our employees to acknowledge ownership by us of inventions conceived as a result of employment from the point of conception and, to the extent necessary, perfect such ownership by assignment, and we require all of our employees, consultants, advisors and any third parties who have access to our trade secrets, proprietary know-how and other confidential information and technology to enter into appropriate confidentiality agreements, we cannot be certain that our trade secrets, proprietary know-how and other confidential information and technology will not be subject to unauthorized disclosure or that our competitors will not otherwise gain access to or independently develop substantially equivalent trade secrets, proprietary know-how and other information and technology. Furthermore, the laws of some foreign countries, in particular, China, where we have operations, do not protect proprietary rights to the same extent or in the same manner as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property globally. If we are unable to prevent unauthorized disclosure of our intellectual property related to our product candidates and technology to third parties, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business and operations.

Intellectual property disputes may be costly, time consuming, and may negatively affect our competitive position.

Our commercial success may depend on our avoiding infringement of the patents and other proprietary rights of third parties as well as on enforcing our patents and other proprietary rights against third parties. Pharmaceutical and biotechnology intellectual property disputes are characterized by complex, lengthy and expensive litigation over patents and other intellectual property rights. We have initiated and may again initiate or become party to or be threatened with future litigation or other proceedings regarding intellectual property rights with respect to our product candidates and competing products.

As our product candidates progress toward commercialization, our collaboration partners or we may be subject to patent infringement claims from third parties. We attempt to ensure that our product candidates do not infringe third-party patents and other proprietary rights. However, the patent landscape in competitive product areas is highly complex, and there may be patents of third parties of which we are unaware that may result in claims of infringement. Accordingly, there can be no assurance that our product candidates do not infringe proprietary rights of third parties, and parties making claims against us may seek and obtain injunctive or other equitable relief, which could potentially block further efforts to develop and commercialize our product candidates including roxadustat or pamrevlumab. Any litigation involving defense against claims of infringement, regardless of the merit of such claims, would involve substantial litigation expense and would be a substantial diversion of management time.

We may consider administrative proceedings and other means for challenging third-party patents and patent applications. An unfavorable outcome in any such challenge could require us to cease using the related technology and to attempt to license rights to it from the prevailing third party, which may not be available on commercially reasonable terms, if at all, in which case our business could be harmed.

We intend, if necessary, to vigorously enforce our intellectual property in order to protect the proprietary position of our product candidates, including roxadustat and pamrevlumab. In addition, our collaboration partners who have been granted licenses to our patents may also have rights related to enforcement of those patents. Active efforts to enforce our patents by us or by our partners may include litigation, administrative proceedings, or both, depending on the potential benefits that might be available from those actions and the costs associated with undertaking those efforts against third parties. We carefully review and monitor publicly available information regarding products that may be competitive with our product candidates and assert our intellectual property rights where appropriate.

Third parties have challenged and may again challenge our patents and patent applications, through interference, reexamination, *inter partes* review, and post-grant review proceedings before the U.S. Patent and Trademark Office ("USPTO") or through comparable proceedings in other territories. For example, various legal challenges against our HIF anemia-related technologies patent portfolio have been filed in several territories including in Europe, the United Kingdom, Canada, and Japan,. Regardless of the final outcome of these actions, the potential narrowing or revocation of any of the HIF anemia-related technology patents does not affect our exclusivity for roxadustat or our freedom-to-operate with respect to use of roxadustat for the treatment of anemia in these or other territories. A settlement has been reached in the litigation in Canada, resulting in the discontinuance of the action and leaving FibroGen's Canadian patents valid and enforceable.

In April 2020, in response to an invalidation action brought against certain of our United Kingdom patents by Akebia, the United Kingdom court handed down a decision invalidating United Kingdom designations of European Patent Nos. 1463823, 1633333, 2298301, 2322153, and 2322155. The United Kingdom designation to European Patent No. 2289531 was held to be valid in amended form, but not infringed by Akebia. We and our partner Astellas have filed an appeal of the decision in the United Kingdom Court of Appeal.

In May 2020, oppositions were filed against our European Patent No. 2872488 (the "'488 Patent"), which claims a crystalline form of roxadustat, and against our European Patent No. 3003284 (the "'284 Patent"), which claims photostable formulations of roxadustat. Final resolution of the opposition proceedings will take time, and we cannot be assured of the breadth of the claims that will remain in the '488 Patent or '284 Patent, or that either or both of the patents will not be revoked in their entirety.

Furthermore, there is a risk that any public announcements concerning the status or outcomes of intellectual property litigation or administrative proceedings may adversely affect the price of our stock. If securities analysts or our investors interpret such status or outcomes as negative or otherwise creating uncertainty, our common stock price may be adversely affected.

Our reliance on third parties and agreements with collaboration partners requires us to share our trade secrets, which increases the possibility that a competitor may discover them or that our trade secrets will be misappropriated or disclosed.

Our reliance on third-party contractors to develop and manufacture our product candidates is based upon agreements that limit the rights of the third parties to use or disclose our confidential information, including our trade secrets and know-how. Despite the contractual provisions, the need to share trade secrets and other confidential information increases the risk that such trade secrets and information are disclosed or used, even if unintentionally, in violation of these agreements. In the highly competitive markets in which our product candidates are expected to compete, protecting our trade secrets, including our strategies for addressing competing products, is imperative, and any unauthorized use or disclosure could impair our competitive position and may have a material adverse effect on our business and operations.

In addition, our collaboration partners are larger, more complex organizations than ours, and the risk of inadvertent disclosure of our proprietary information may be increased despite their internal procedures and contractual obligations that we have in place with them. Despite our efforts to protect our trade secrets and other confidential information, a competitor's discovery of such trade secrets and information could impair our competitive position and have an adverse impact on our business.

The cost of maintaining our patent protection is high and requires continuous review and diligence. We may not be able to effectively maintain our intellectual property position throughout the major markets of the world.

The USPTO and foreign patent authorities require maintenance fees and payments as well as continued compliance with a number of procedural and documentary requirements. Noncompliance may result in abandonment or lapse of the subject patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance may result in reduced royalty payments for lack of patent coverage in a particular jurisdiction from our collaboration partners or may result in competition, either of which could have a material adverse effect on our business.

We have made, and will continue to make, certain strategic decisions in balancing costs and the potential protection afforded by the patent laws of certain countries. As a result, we may not be able to prevent third parties from practicing our inventions in all countries throughout the world, or from selling or importing products made using our inventions in and into the U.S. or other countries. Third parties may use our technologies in territories in which we have not obtained patent protection to develop their own products and, further, may infringe our patents in territories which provide inadequate enforcement mechanisms, even if we have patent protection. Such third-party products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

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The laws of some foreign countries do not protect proprietary rights to the same extent as do the laws of the U.S., and we may encounter significant problems in securing and defending our intellectual property rights outside the U.S.

Many companies have encountered significant problems in protecting and defending intellectual property rights in certain countries. The legal systems of certain countries do not always favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to pharmaceutical and biotechnology products, which could make it difficult for us to stop infringement of our patents, misappropriation of our trade secrets, or marketing of competing products in violation of our proprietary rights. In China, our intended establishment of significant operations will depend in substantial part on our ability to effectively enforce our intellectual property rights in that country. Proceedings to enforce our intellectual property rights in foreign countries could result in substantial costs and divert our efforts and attention from other aspects of our business, and could put our patents in these territories at risk of being invalidated or interpreted narrowly, or our patent applications at risk of not being granted, and could provoke third parties to assert claims against us. We may not prevail in all legal or other proceedings that we may initiate and, if we were to prevail, the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Intellectual property rights do not address all potential threats to any competitive advantage we may have.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and intellectual property rights may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- Others may be able to make compounds that are the same as or similar to our current or future product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed.
- We or any of our licensors or strategic partners might not have been the first to file patent applications covering certain of our inventions.
- Others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- The prosecution of our pending patent applications may not result in granted patents.
- Granted patents that we own or have exclusively licensed may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors.
- Patent protection on our product candidates may expire before we are able to develop and commercialize the product, or before we are able to recover our investment in the product.
- Our competitors might conduct research and development activities in the U.S. and other countries that provide a safe harbor from patent infringement claims for such activities, as well as in countries in which we do not have patent rights, and may then use the information learned from such activities to develop competitive products for sale in markets where we intend to market our product candidates.

The existence of counterfeit pharmaceutical products in pharmaceutical markets may compromise our brand and reputation and have a material adverse effect on our business, operations and prospects.

Counterfeit products, including counterfeit pharmaceutical products, are a significant problem, particularly in China. Counterfeit pharmaceuticals are products sold or used for research under the same or similar names, or similar mechanism of action or product class, but which are sold without proper licenses or approvals, and are often lower cost, lower quality, different potency, or have different ingredients or formulations, and have the potential to damage the reputation for quality and effectiveness of the genuine product. Such products may be used for indications or purposes that are not recommended or approved or for which there is no data or inadequate data with regard to safety or efficacy. Such products divert sales from genuine products. If counterfeit pharmaceuticals illegally sold or used for research result in adverse events or side effects to consumers, we may be associated with any negative publicity resulting from such incidents. Consumers may buy counterfeit pharmaceuticals that are in direct competition with our pharmaceuticals, which could have an adverse impact on our revenues, business and results of operations. In addition, the use of counterfeit products could be used in non-clinical or clinical studies, or could otherwise produce undesirable side effects or adverse events that may be attributed to our products as well, which could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in the delay or denial of regulatory approval by the FDA or other regulatory authorities and potential product liability claims. With respect to China, although the government has recently been increasingly active in policing counterfeit pharmaceuticals, there is not yet an effective counterfeit pharmaceutical regulation control and enforcement system in China. As a result, we may not be able to prevent third parties from selling or purporting to sell our products in China. The proliferation of counterfeit pharmaceuticals has grown in recent years and may continue to grow in the future. The existence of and any increase in the sales and production of counterfeit pharmaceuticals, or the technological capabilities of counterfeiters, could negatively impact our revenues, brand reputation, business and results of operations.

Risks Related to Government Regulation

The regulatory approval process is highly uncertain and we may not obtain regulatory approval for our product candidates.

The time required to obtain approval by the FDA and comparable foreign regulatory authorities is unpredictable, but typically takes many years following the commencement of preclinical studies and clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. In addition, approval policies, regulations, or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions. Except for roxadustat in China, Japan, and Chile for patients on dialysis and not on dialysis, we have not obtained regulatory approval for any product candidate, and it is possible that neither roxadustat nor pamrevlumab, nor any future product candidates we may discover, in-license or acquire and seek to develop in the future, will obtain regulatory approval in additional countries.

Our product candidates could fail to receive regulatory approval from the FDA or other regulatory authorities for many reasons, including:

- disagreement over the design or implementation of our clinical trials;
- failure to demonstrate that a product candidate is safe and effective for its proposed indication;
- failure of clinical trials to meet the level of statistical significance required for approval;
- failure to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- disagreement over our interpretation of data from preclinical studies or clinical trials;
- disagreement over whether to accept efficacy results from clinical trial sites outside the U.S. where the standard of care is potentially different from that in the U.S.;
- the insufficiency of data collected from clinical trials of our present or future product candidates to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- disapproval of the manufacturing processes or facilities of either our manufacturing plant or third party manufacturers with whom we contract for clinical and commercial supplies; or
- · changes in the approval policies or regulations that render our preclinical and clinical data insufficient for approval.

The FDA or other regulatory authorities may require more information, including additional preclinical or clinical data to support approval, or different analyses, which may delay or prevent approval and our commercialization plans, or we may decide to abandon the development program altogether. Even if we do obtain regulatory approval, our product candidates may be approved for fewer or more limited indications than we request, approval may be contingent on the performance of costly post-marketing clinical trials, or approval may require labeling that does not include the labeling claims necessary or desirable for the successful commercialization of that product candidate. In addition, if our product candidates produce undesirable side effects or safety issues, the FDA may require the establishment of REMS or other regulatory authorities may require the establishment of a similar strategy, that may restrict distribution of our approved products, if any, and impose burdensome implementation requirements on us. Any of the foregoing scenarios could materially harm the commercial prospects for our product candidates.

Even if we believe our clinical trials are successful, regulatory authorities may not agree that our completed clinical trials provide adequate data on safety or efficacy. Approval by one regulatory authority does not ensure approval by any other regulatory authority. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. We may not be able to file for regulatory approvals and even if we file we may not receive the necessary approvals to commercialize our product candidates in any market.

Our current and future relationships with customers, physicians, and third-party payors are subject to healthcare fraud and abuse laws, false claims laws, transparency laws, privacy and security laws, and other regulations. If we are unable to comply with such laws, we could face substantial penalties.

Our current and future relationships with customers, physicians, and third-party payors are subject to health care laws and regulations, which may constrain the business or financial arrangements and relationships through which we research, as well as, sell, market and distribute any products for which we obtain marketing approval. If we obtain approval in the U.S. for any of our product candidates, the regulatory requirements applicable to our operations, in particular our sales and marketing efforts, will increase significantly with respect to our operations and the potential for administrative, civil and criminal enforcement by the federal government and the states and foreign governments will increase with respect to the conduct of our business. The laws that may affect our operations in the U.S. include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering
 or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable
 under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by Health Information Technology and Clinical Health Act, and its implementing regulations, which imposes certain
 requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business
 associates that perform services for them that involve the use, or disclosure of, individually identifiable health information as well as their
 covered subcontractors relating to the privacy, security, and transmission of individually identifiable health information;
- the federal physician sunshine requirements under the Patient Protection and Affordable Care Act, as amended by the Health Care and
 Education Reconciliation Act of 2010 (collectively, the "PPACA"), which requires manufacturers of drugs, devices, biologics, and medical
 supplies to report annually to the Centers for Medicare & Medicaid Services ("CMS"), information related to payments and other transfers
 of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and
 other healthcare providers and their immediate family members;

- foreign and state law equivalents of each of the above federal laws, such as the U.S. Foreign Corrupt Practices Act ("FCPA"), anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts; and
- the Trade Agreements Act ("TAA"), which requires that drugs sold to the U.S. Government must be manufactured in the U.S. or in TAA approved and designated countries. Drugs manufactured in countries not approved under the TAA, may not be sold to the U.S. without specific regulatory approval. We have little experience with this regulation and there is a risk that drugs made from Chinese-made API may not be sold to an entity of the U.S. such as the Veterans Health Administration ("VA") due to our inability to obtain regulatory approval. While there have been recent VA policy changes that appear to allow for sale of drugs from non-TAA approved countries, this policy may change or there may be additional policies or legislation that affect our ability to sell drug to the U.S. Government.

The scope of these laws and our lack of experience in establishing the compliance programs necessary to comply with this complex and evolving regulatory environment increases the risks that we may unknowingly violate the applicable laws and regulations. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, disgorgement, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could materially adversely affect our ability to operate our business and our financial results.

Even if resolved in our favor, litigation or other legal proceedings relating to healthcare laws and regulations may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development, manufacturing, sales, marketing or distribution activities. Uncertainties resulting from the initiation and continuation of litigation or other proceedings relating to applicable healthcare laws and regulations could have a material adverse effect on our ability to compete in the marketplace.

We are subject to laws and regulations governing corruption, which will require us to maintain costly compliance programs.

We must comply with a wide range of laws and regulations to prevent corruption, bribery, and other unethical business practices, including the FCPA, anti-bribery and anti-corruption laws in other countries, particularly China. The implementation and maintenance of compliance programs is costly and such programs may be difficult to enforce, particularly where reliance on third parties is required.

Anti-bribery laws prohibit us, our employees, and some of our agents or representatives from offering or providing any personal benefit to covered government officials to influence their performance of their duties or induce them to serve interests other than the missions of the public organizations in which they serve. Certain commercial bribery rules also prohibit offering or providing any personal benefit to employees and representatives of commercial companies to influence their performance of their duties or induce them to serve interests other than their employers. The FCPA also obligates companies whose securities are listed in the U.S. to comply with certain accounting provisions requiring us to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the Department of Justice. The SEC is involved with enforcement of the books and records provisions of the FCPA.

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Compliance with these anti-bribery laws is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the anti-bribery laws present particular challenges in the pharmaceutical industry because in many countries including China, hospitals are state-owned or operated by the government, and doctors and other hospital employees are considered foreign government officials. Furthermore, in certain countries (China in particular), hospitals and clinics are permitted to sell pharmaceuticals to their patients and are primary or significant distributors of pharmaceuticals. Certain payments to hospitals in connection with clinical studies, procurement of pharmaceuticals and other work have been deemed to be improper payments to government officials that have led to vigorous anti-bribery law enforcement actions and heavy fines in multiple jurisdictions, particularly in the U.S. and China.

It is not always possible to identify and deter violations, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations.

In the pharmaceutical industry, corrupt practices include, among others, acceptance of kickbacks, bribes or other illegal gains or benefits by the hospitals and medical practitioners from pharmaceutical manufacturers, distributors or their third-party agents in connection with the prescription of certain pharmaceuticals. If our employees, affiliates, distributors or third-party marketing firms violate these laws or otherwise engage in illegal practices with respect to their sales or marketing of our products or other activities involving our products, we could be required to pay damages or heavy fines by multiple jurisdictions where we operate, which could materially and adversely affect our financial condition and results of operations. The Chinese government has also sponsored anti-corruption campaigns from time to time, which could have a chilling effect on any future marketing efforts by us to new hospital customers. There have been recent occurrences in which certain hospitals have denied access to sales representatives from pharmaceutical companies because the hospitals wanted to avoid the perception of corruption. If this attitude becomes widespread among our potential customers, our ability to promote our products to hospitals may be adversely affected.

As we expand our operations in China and other jurisdictions internationally, we will need to increase the scope of our compliance programs to address the risks relating to the potential for violations of the FCPA and other anti-bribery and anti-corruption laws. Our compliance programs will need to include policies addressing not only the FCPA, but also the provisions of a variety of anti-bribery and anti-corruption laws in multiple foreign jurisdictions, including China, provisions relating to books and records that apply to us as a public company, and include effective training for our personnel throughout our organization. The creation and implementation of anti-corruption compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required. Violation of the FCPA and other anti-corruption laws can result in significant administrative and criminal penalties for us and our employees, including substantial fines, suspension or debarment from government contracting, prison sentences, or even the death penalty in extremely serious cases in certain countries. The SEC also may suspend or bar us from trading securities on U.S. exchanges for violation of the FCPA's accounting provisions. Even if we are not ultimately punished by government authorities, the costs of investigation and review, distraction of our personnel, legal defense costs, and harm to our reputation could be substantial and could limit our profitability or our ability to develop or commercialize our product candidates. In addition, if any of our competitors are not subject to the FCPA, they may engage in practices that will lead to their receipt of preferential treatment from foreign hospitals and enable them to secure business from foreign hospitals in ways that are unavailable to us.

We have identified material weaknesses in our internal control over financial reporting. If we are unable to remediate these, or if we otherwise fail to maintain an effective system of internal control, it may result in material misstatements in our financial statements.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting and for evaluating and reporting on the effectiveness of our system of internal control. Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of financial statements for external reporting purposes in accordance with generally accepted accounting principles. As a public company, we are required to comply with the Sarbanes-Oxley Act and other rules that govern public companies.

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As of September 30, 2020, we have identified a material weakness in the risk assessment component of internal control as we did not appropriately design and maintain an effective risk assessment process at a precise enough level to identify new and evolving risks of material misstatement to the financial statements as a result of changes in our business operation. This material weakness gave rise to the following additional control deficiencies, which we also determined to be material weaknesses. We did not design and maintain effective controls related to the timely identification of shipments associated with drug product revenue and we did not design and maintain effective controls related to the timely identification of changes in estimated variable consideration related to drug product revenue. Each of these material weaknesses could result in material misstatements in the drug product revenue, contract asset, or contract liability account balances or disclosures in our annual or interim consolidated financial statements that would not be prevented or detected. The material weaknesses described above did not result in any material misstatements of our consolidated financial statements or disclosures, but did result in immaterial out-of-period adjustments to drug product revenue related to pre-commercial shipments of drug product, contract assets and contract liabilities, and related financial statement disclosures during the quarter ended September 30, 2020.

We have developed a detailed remediation plan and are making progress to improve our related internal control over financial reporting. For further discussion of the material weaknesses identified and our remedial efforts, see Part II, Item 9A, "Controls and Procedures" in this Annual Report on Form 10-K.

Remediation efforts place a significant burden on management and add increased pressure on our financial resources and processes. If we are unable to successfully remediate our existing or any future material weaknesses or other deficiencies in our internal control over financial reporting, the accuracy and timing of our financial reporting may be adversely affected, our liquidity, our access to capital markets may be adversely affected, we may be unable to maintain or regain compliance with applicable securities laws, and the NASDAQ Stock Market LLC listing requirements, we may be subject to regulatory investigations and penalties, investors may lose confidence in our financial reporting, and our stock price may decline.

The impact of recent U.S. healthcare reform, its potential partial or full repeal, and other changes in the healthcare industry and in healthcare spending is currently unknown, and may adversely affect our business model.

The commercial potential for our approved products could be affected by changes in healthcare spending and policy in the U.S. and abroad. We operate in a highly regulated industry and new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to healthcare availability, the method of delivery or payment for healthcare products and services could negatively impact our business, operations and financial condition.

In the U.S., the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 ("MMA") altered Medicare coverage and payments for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. The MMA also provided authority for limiting the number of drugs that will be covered in any therapeutic class and as a result, we expect that there will be additional pressure to reduce costs. For example, the CMS in implementing the MMA has enacted regulations that reduced capitated payments to dialysis providers. These cost reduction initiatives and other provisions of the MMA could decrease the scope of coverage and the price that may be received for any approved dialysis products and could seriously harm our business and financial condition. While the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policies and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may cause a similar reduction in payments from private payors. Similar regulations or reimbursement policies have been enacted in many international markets that could similarly impact the commercial potential for our products.

Under the Medicare Improvements for Patients and Providers Act ("MIPPA"), a basic case-mix adjusted composite, or bundled, payment system commenced in January 2011 and transitioned fully by January 2014 to a single reimbursement rate for drugs and all services furnished by renal dialysis centers for Medicare beneficiaries with end-stage renal disease. Specifically, under MIPPA the End-Stage Renal Disease Prospective Payment System (the "ESRD PPS") bundle now covers drugs, services, lab tests and supplies under a single treatment base rate for reimbursement by the CMS based on the average cost per treatment, including the cost of ESAs and IV iron doses, typically without adjustment for usage. It is unknown whether roxadustat, if approved in the U.S., will be included in the payment bundle or the timing of inclusion. Under MIPPA, agents that have no IV equivalent in the bundle are currently expected to be excluded from the bundle until 2025. If roxadustat were included in the bundle, it may reduce the price that could be charged for roxadustat, and therefore potentially limit our profitability. Based on roxadustat's differentiated mechanism of action and therapeutic effects, and discussions with our collaboration partner, we currently believe that roxadustat might not initially be included in the bundle and would instead be eligible for a Transitional Drug Add-on Payment Adjustment ("TDAPA") for a 24-month period. At the 24-month mark, CMS would determine if the TDAPA period should be extended for roxadustat or ended. When the TDAPA period ends, CMS will determine if roxadustat should be included in the bundle and, if so, what changes to the ESRD PPS reimbursement should be made. If roxadustat is included in the ESRD PPS bundle, it may have an impact on roxadustat pricing within Dialysis Organizations. If roxadustat is not included in the bundle after the TDAPA period, and would therefore be reimbursed outside of the bundle, it may potentially limit further market penetration of roxadustat. We currently expect roxadustat to be granted TDAPA designation either July 1 or October 1 of 2021. However, there is a risk that we do not receive TDAPA designation, or when we expect it, in which case, there would be a significant impact on roxadustat revenue in 2021, or until TDAPA designation is granted.

In March 2010, the PPACA was passed, which substantially changed the way healthcare is financed by both governmental and private payors in the U.S. There remain judicial and Congressional challenges to certain aspects of the PPACA. For example, the Tax Cuts and Jobs Act of 2017, (the "Tax Act"), was enacted, which includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. Additionally, on December 14, 2018, a Texas U.S. District Court Judge ruled that the PPACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the PPACA are invalid as well. The U.S. Supreme Court is currently reviewing this case, but it is unknown when a decision will be reached. Although the U.S. Supreme Court has yet ruled on the constitutionality of the PPACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the PPACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the PPACA. It is unclear how the U.S. Supreme Court ruling, other such litigation, and the healthcare reform measures of the Biden administration will impact the PPACA and our business.

Further, in the U.S. there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under government payor programs, and review the relationship between pricing and manufacturer patient programs. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempt to implement several of the administration's proposals. The FDA also released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed pending review by the Biden administration until March 22, 2021. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. On December 28, 2020, the U.S. District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. However, it is unclear whether the Biden administration will work to reverse these measures or pursue similar policy initiatives. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. We expect that additional U.S. healthcare reform measures will be adopted in the future, any of which could limit the amounts that the U.S. federal government will pay for healthcare products and services, which could result in reduced demand for any future products or additional pricing pressures.

Roxadustat is considered a Class 2 substance on the 2019 World Anti-Doping Agency Prohibited List that could limit sales and increase security and distribution costs for our partners and us.

Roxadustat is considered a Class 2 substance on the World Anti-Doping Agency Prohibited List. There are enhanced security and distribution procedures we and our collaboration partners and third-party contractors will have to take to limit the risk of loss of product in the supply chain. As a result, our distribution, manufacturing and sales costs for roxadustat, as well as for our partners, will be increased which will reduce profitability. In addition, there is a risk of reduced sales due to patient access to this drug.

Our employees may engage in misconduct or improper activities, which could result in significant liability or harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failure to:

- comply with FDA regulations or similar regulations of comparable foreign regulatory authorities;
- provide accurate information to the FDA or comparable foreign regulatory authorities;
- · comply with manufacturing standards we have established;
- comply with privacy laws protecting personal information;
- comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities;
- comply with the FCPA and other anti-bribery laws;
- report financial information or data accurately; or
- disclose unauthorized activities to us.

Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions, delays in clinical trials, or serious harm to our reputation. We have adopted a code of conduct for our directors, officers and employees, but it is not always possible to identify and deter employee misconduct. The precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could harm our business, results of operations, financial condition and cash flows, including through the imposition of significant fines or other sanctions.

If we fail to comply with environmental, health or safety laws and regulations, we could incur fines, penalties or other costs.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations applicable to our operations in the U.S. and foreign countries. These current or future laws and regulations may impair our research, development or manufacturing efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Risks Related to Our International Operations

We have established operations in China and are seeking approval to commercialize our product candidates outside of the U.S., and a number of risks associated with international operations could materially and adversely affect our business.

We expect to be subject to a number of risks related with our international operations, many of which may be beyond our control. These risks include:

- different regulatory requirements for drug approvals in different countries;
- different standards of care in various countries that could complicate the evaluation of our product candidates;
- different U.S. and foreign drug import and export rules;
- reduced protection for intellectual property rights in certain countries;
- · changes in tariffs, trade barriers and regulatory requirements;
- different reimbursement systems and different competitive drugs indicated to treat the indications for which our product candidates are being developed;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- compliance with the FCPA, and other anti-corruption and anti-bribery laws;
- U.S. and foreign taxes, including income, excise, customs, consumption, withholding, and payroll taxes;
- foreign currency fluctuations, which could result in increased operating costs and expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;

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- a reliance on CROs, clinical trial sites, principal investigators and other third parties that may be less experienced with clinical trials or have different methods of performing such clinical trials than we are used to in the U.S.;
- potential liability resulting from development work conducted by foreign distributors; and
- business interruptions resulting from geopolitical actions specific to an international region, including war and terrorism, or natural disasters, including the differing impact of the COVID-19 pandemic on each region.

The pharmaceutical industry in China is highly regulated and such regulations are subject to change.

The pharmaceutical industry in China is subject to comprehensive government regulation and supervision, encompassing the approval, registration, manufacturing, packaging, licensing and marketing of new drugs. In recent years, many aspects of pharmaceutical industry regulation have undergone significant reform, and reform may continue. For example, the Chinese government implemented regulations that impact distribution of pharmaceutical products in China, where at most two invoices may be issued throughout the distribution chain, a change that required us to change our distribution paradigm. Any regulatory changes or amendments may result in increased compliance costs to our business or cause delays in or prevent the successful development or commercialization of our product candidates in China. Any failure by us or our partners to maintain compliance with applicable laws and regulations or obtain and maintain required licenses and permits may result in the suspension or termination of our business activities in China.

We have limited experience distributing drugs in China.

We have established a jointly owned entity with AstraZeneca in China, one that has a distribution license. It is subject to a new body of regulations pertaining to distribution with which we have limited experience. This new distribution structure may impose higher costs or limit or delay our ability to sell products to our principal customers, and may limit the near term sales of our products. There are operational risks associated with the jointly owned entity, such as working capital funding requirements and regulatory challenges, which could impact our ability to operate in China, including increasing sales of roxadustat. We have limited experience managing distribution of pharmaceutical products, and this new distribution structure may impose higher costs or limit or delay our ability to sell products to our principal customers, and may limit the near term sales of our products.

We use our own manufacturing facilities in China to produce roxadustat API and drug product. There are risks inherent to operating commercial manufacturing facilities, and with these being our single source suppliers, we may not be able to continually meet market demand.

We have two manufacturing facilities in China, with one located in Beijing and the other in Cangzhou, Hebei.

We will be obligated to comply with continuing cGMP requirements and there can be no assurance that we will maintain all of the appropriate licenses required to manufacture our product candidates for clinical and commercial use in China. In addition, we and our product suppliers must continually spend time, money and effort in production, record-keeping and quality assurance and appropriate controls in order to ensure that any products manufactured in our facilities meet applicable specifications and other requirements for product safety, efficacy and quality and there can be no assurance that our efforts will continue to be successful in meeting these requirements.

Manufacturing facilities in China are subject to periodic unannounced inspections by the NMPA and other regulatory authorities. We expect to depend on these facilities for our product candidates and business operations in China, and we do not yet have a secondary source supplier for either roxadustat API or drug product in China. Natural disasters or other unanticipated catastrophic events, including power interruptions, water shortages, storms, fires, pandemics (including the COVID-19 pandemic), earthquakes, terrorist attacks, government appropriation of our facilities, and wars, could significantly impair our ability to operate our manufacturing facilities. Certain equipment, records and other materials located in these facilities would be difficult to replace or would require substantial replacement lead-time that would impact our ability to successfully commercialize our product candidates in China. The occurrence of any such event could materially and adversely affect our business, financial condition, results of operations, cash flows and prospects.

As a company, we have limited experience in pharmacovigilance, medical affairs, and management of the third-party distribution logistics, and cannot assure you we will be able to meet regulatory requirements or operate in these capacities successfully.

We are responsible for commercial manufacturing, pharmacovigilance, medical affairs, and management of the third-party distribution logistics (with AstraZeneca through a jointly owned entity that will perform roxadustat distribution) for roxadustat commercial activities in China. While we have been increasing our staffing in these areas, as a company, we have no experience managing or operating these functions for a commercial product and there can be no guarantee that we will do so efficiently or effectively. Mistakes or delays in these areas could limit our ability to successfully commercialize roxadustat in China, could limit our eventual market penetration, sales and profitability, and could subject us to significant liability in China.

We and our collaboration partner in China, AstraZeneca, may experience difficulties in successfully growing and sustaining sales of roxadustat in China.

We and AstraZeneca have a profit sharing arrangement with respect to roxadustat in China and any difficulties we may experience in growing and sustaining sales will affect our bottom line. Difficulties may be related to our ability to maintain reasonable pricing and reimbursement, obtain hospital listing, or other difficulties related to distribution, marketing, and sales efforts in China. For example, our current National Reimbursement Drug List reimbursement pricing is effective for a standard two-year period (between January 1, 2020 to December 31, 2021), after which time we will have to renegotiate a new price for roxadustat, which we expect to be lower based upon historical precedents. Sales of roxadustat in China may ultimately be limited due to the complex nature of the healthcare system, low average personal income, pricing controls, still developing infrastructure and potentially rapid competition from other products.

The retail prices of any product candidates that we develop may be subject to pricing control in China and elsewhere.

The price for pharmaceutical products is highly regulated in China, both at the national and provincial level. Price controls may reduce prices to levels significantly below those that would prevail in less regulated markets or limit the volume of products that may be sold, either of which may have a material and adverse effect on potential revenues from sales of roxadustat in China. Moreover, the process and timing for the implementation of price restrictions is unpredictable, which may cause potential revenues from the sales of roxadustat to fluctuate from period to period.

FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") would be subject to restrictions on paying dividends or making other payments to us, which may restrict our ability to satisfy our liquidity requirements.

We plan to conduct all of our business in China through FibroGen China Anemia Holdings, Ltd. and FibroGen Beijing. We may rely on dividends and royalties paid by FibroGen Beijing for a portion of our cash needs, including the funds necessary to service any debt we may incur and to pay our operating costs and expenses. The payment of dividends by FibroGen Beijing is subject to limitations. Regulations in China currently permit payment of dividends only out of accumulated profits as determined in accordance with accounting standards and regulations in China. FibroGen Beijing is not permitted to distribute any profits until losses from prior fiscal years have been recouped and in any event must maintain certain minimum capital requirements. FibroGen Beijing is also required to set aside at least 10.0% of its after-tax profit based on Chinese accounting standards each year to its statutory reserve fund until the cumulative amount of such reserves reaches 50.0% of its registered capital. Statutory reserves are not distributable as cash dividends. In addition, if FibroGen Beijing incurs debt on its own behalf in the future, the agreements governing such debt may restrict its ability to pay dividends or make other distributions to us. As of December 31, 2020, approximately \$44.6 million of our cash and cash equivalents is held in China.

Any capital contributions from us to FibroGen Beijing must be approved by the Ministry of Commerce in China, and failure to obtain such approval may materially and adversely affect the liquidity position of FibroGen Beijing.

The Ministry of Commerce in China or its local counterpart must approve the amount and use of any capital contributions from us to FibroGen Beijing, and there can be no assurance that we will be able to complete the necessary government registrations and obtain the necessary government approvals on a timely basis, or at all. If we fail to do so, we may not be able to contribute additional capital to fund our Chinese operations, and the liquidity and financial position of FibroGen Beijing may be materially and adversely affected.

We may be subject to currency exchange rate fluctuations and currency exchange restrictions with respect to our operations in China, which could adversely affect our financial performance.

Most of our product sales will occur in local Chinese currency and our operating results will be subject to volatility from currency exchange rate fluctuations. To date, we have not hedged against the risks associated with fluctuations in exchange rates and, therefore, exchange rate fluctuations could have an adverse impact on our future operating results. Changes in value of the Renminbi against the U.S. dollar, Euro and other currencies is affected by, among other things, changes in China's political and economic conditions. Currently, the Renminbi is permitted to fluctuate within a narrow and managed band against a basket of certain foreign currencies. Any significant currency exchange rate fluctuations may have a material adverse effect on our business and financial condition.

In addition, the Chinese government imposes controls on the convertibility of the Renminbi into foreign currencies and the remittance of foreign currency out of China for certain transactions. Shortages in the availability of foreign currency may restrict the ability of FibroGen Beijing to remit sufficient foreign currency to pay dividends or other payments to us, or otherwise satisfy their foreign currency-denominated obligations. Under existing Chinese foreign exchange regulations, payments of current account items, including profit distributions, interest payments and balance of trade, can be made in foreign currencies without prior approval from the State Administration of Foreign Exchange by complying with certain procedural requirements. However, approval from State Administration of Foreign Exchange or its local branch is required where Renminbi is to be converted into foreign currency and remitted out of China to pay capital expenses such as the repayment of loans denominated in foreign currencies. The Chinese government may also at its discretion restrict access in the future to foreign currencies for current account transactions. If the foreign exchange control system prevents us from obtaining sufficient foreign currency to satisfy our operational requirements, our liquidity and financial position may be materially and adversely affected.

Because FibroGen Beijing's funds are held in banks that do not provide insurance, the failure of any bank in which FibroGen Beijing deposits its funds could adversely affect our business.

Banks and other financial institutions in China do not provide insurance for funds held on deposit. As a result, in the event of a bank failure, FibroGen Beijing may not have access to funds on deposit. Depending upon the amount of money FibroGen Beijing maintains in a bank that fails, its inability to have access to cash could materially impair its operations.

We may be subject to tax inefficiencies associated with our offshore corporate structure.

The tax regulations of the U.S. and other jurisdictions in which we operate are extremely complex and subject to change. New laws, new interpretations of existing laws, such as the Base Erosion Profit Shifting project initiated by the Organization for Economic Co-operation and Development, and any legislation proposed by the relevant taxing authorities, or limitations on our ability to structure our operations and intercompany transactions may lead to inefficient tax treatment of our revenue, profits, royalties, and distributions, if any are achieved.

In addition, our foreign subsidiaries and we have various intercompany transactions. We may not be able to obtain certain benefits under relevant tax treaties to avoid double taxation on certain transactions among our subsidiaries. If we are not able to avail ourselves to the tax treaties, we could be subject to additional taxes, which could adversely affect our financial condition and results of operations.

On December 22, 2017, the Tax Cuts and Jobs Act (Tax Act) was enacted which instituted various changes to the taxation of multinational corporations. Since inception, various regulations and interpretations have been issued by governing authorities and we continue to examine the impacts to our business, which could potentially have a material adverse effect on our business, results of operations or financial conditions.

Our foreign operations, particularly those in China, are subject to significant risks involving the protection of intellectual property.

We seek to protect the products and technology that we consider important to our business by pursuing patent applications in China and other countries, relying on trade secrets or pharmaceutical regulatory protection or employing a combination of these methods. We note that the filing of a patent application does not mean that we will be granted a patent, or that any patent eventually granted will be as broad as requested in the patent application or will be sufficient to protect our technology. There are a number of factors that could cause our patents, if granted, to become invalid or unenforceable or that could cause our patent applications not to be granted, including known or unknown prior art, deficiencies in the patent application, or lack of originality of the technology. Furthermore, the terms of our patents are limited. The patents we hold and the patents that may be granted from our currently pending patent applications have, absent any patent term adjustment or extension, a twenty-year protection period starting from the date of application.

Intellectual property rights and confidentiality protections in China may not be as effective as those in the U.S. or other countries for many reasons, including lack of procedural rules for discovery and evidence, low damage awards, and lack of judicial independence. Implementation and enforcement of China intellectual property laws have historically been deficient and ineffective and may be hampered by corruption and local protectionism. Policing unauthorized use of proprietary technology is difficult and expensive, and we may need to resort to litigation to enforce or defend patents issued to us or to determine the enforceability and validity of our proprietary rights or those of others. The experience and capabilities of China courts in handling intellectual property litigation varies and outcomes are unpredictable. An adverse determination in any such litigation could materially impair our intellectual property rights and may harm our business.

Uncertainties with respect to the China legal system could have a material adverse effect on us.

The legal system of China is a civil law system primarily based on written statutes. Unlike in a common law system, prior court decisions may be cited for reference but are not binding. Because the China legal system continues to rapidly evolve, the interpretations of many laws, regulations and rules are not always uniform and enforcement of these laws, regulations and rules involve uncertainties, which may limit legal protections available to us. Moreover, decision makers in the China judicial system have significant discretion in interpreting and implementing statutory and contractual terms, which may render it difficult for FibroGen Beijing to enforce the contracts it has entered into with our business partners, customers and suppliers. Different government departments may have different interpretations of certain laws and regulations, and licenses and permits issued or granted by one government authority may be revoked by a higher government authority at a later time. Navigating the uncertainty and change in the China legal system will require the devotion of significant resources and time, and there can be no assurance that our contractual and other rights will ultimately be enforced.

Changes in China's economic, governmental, or social conditions could have a material adverse effect on our business.

Chinese society and the Chinese economy continue to undergo significant change. Changes in the regulatory structure, regulations, and economic policies of the Chinese government could have a material adverse effect on the overall economic growth of China, which could adversely affect our ability to conduct business in China. The Chinese government continues to adjust economic policies to promote economic growth. Some of these measures benefit the overall Chinese economy, but may also have a negative effect on us. For example, our financial condition and results of operations in China may be adversely affected by government control over capital investments or changes in tax regulations. As the Chinese pharmaceutical industry grows and evolves, the Chinese government may also implement measures to change the regulatory structure and structure of foreign investment in this industry. We are unable to predict the frequency and scope of such policy changes and structural changes, any of which could materially and adversely affect FibroGen Beijing's development and commercialization timelines, liquidity, access to capital, and its ability to conduct business in China. Any failure on our part to comply with changing government regulations and policies could result in the loss of our ability to develop and commercialize our product candidates in China. In addition, the changing government regulations and policies could result in delays and cost increases to our development, manufacturing, approval, and commercialization timelines in China.

Our operations in China subject us to various Chinese labor and social insurance laws, and our failure to comply with such laws may materially and adversely affect our business, financial condition and results of operations.

We are subject to China Labor Contract Law, which provides strong protections for employees and imposes many obligations on employers. The Labor Contract Law places certain restrictions on the circumstances under which employers may terminate labor contracts and require economic compensation to employees upon termination of employment, among other things. In addition, companies operating in China are generally required to contribute to labor union funds and the mandatory social insurance and housing funds. Any failure by us to comply with Chinese labor and social insurance laws may subject us to late fees, fines and penalties, or cause the suspension or termination of our ability to conduct business in China, any of which could have a material and adverse effect on business, results of operations and prospects.

Risks Related to the Operation of Our Business

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future and may never achieve or sustain profitability. We may require additional financings in order to fund our operations.

We are a biopharmaceutical company with two lead product candidates in clinical development, roxadustat for anemia in CKD, myelodysplastic syndromes, and chemotherapy-induced anemia, and pamrevlumab for IPF, pancreatic cancer, and DMD. Most of our revenue generated to date has been based on our collaboration agreements and we have limited commercial drug product sales to date. We continue to incur significant research and development and other expenses related to our ongoing operations. Our net loss for the year ended December 31, 2020, 2019 and 2018 were \$189.3 million, \$77.0 million and \$86.4 million, respectively. As of December 31, 2020, we had an accumulated deficit of \$974.0 million. As of December 31, 2020, we had capital resources consisting of cash, cash equivalents and short-term investments of \$686.5 million plus \$0.2 million of long-term investments classified as available for sale securities. Despite contractual development and cost coverage commitments from our collaboration partners, AstraZeneca and Astellas, and the potential to receive milestone and other payments from these partners, and despite commercialization efforts in the China and Japan for roxadustat for the treatment of anemia caused by CKD, we anticipate we will continue to incur losses on an annual basis for the foreseeable future. If we do not successfully develop and continue to obtain regulatory approval for our existing or any future product candidates and effectively manufacture, market and sell the product candidates that are approved, we may never achieve or sustain profitability on a quarterly or annual basis. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. Our failure to become and remain profitable would depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations.

We believe that we will continue to expend substantial resources for the foreseeable future as we continue late-stage clinical development of roxadustat, grow our operations in China, expand our clinical development efforts on pamrevlumab, continue to seek regulatory approval, establish commercialization capabilities of our product candidates, and pursue additional indications. These expenditures will include costs associated with research and development, conducting preclinical trials and clinical trials, obtaining regulatory approvals in various jurisdictions, and manufacturing and supplying products and product candidates for ourselves and our partners. The outcome of any clinical trial and/or regulatory approval process is highly uncertain and we are unable to fully estimate the actual costs necessary to successfully complete the development and regulatory approval process for our compounds in development and any future product candidates. We believe that the net proceeds from our 2017 public offerings, our existing cash and cash equivalents, short-term and long-term investments and accounts receivable, and expected third-party collaboration revenues will allow us to fund our operating plans through at least the next 12 months. Our operating plans or third-party collaborations may change as a result of many factors, including the success of our development and commercialization efforts, operations costs (including manufacturing and regulatory), competition, and other factors that may not currently be known to us, and we therefore may need to seek additional funds sooner than planned, through offerings of public or private securities, debt financings or other sources, such as royalty monetization or other structured financings. Such financings may result in dilution to stockholders, imposition of debt covenants and repayment obligations, or other restrictions that may adversely affect our business. We may also seek additional capital due to favorable market conditions or strategic considerations even if we c

Additional funds may not be available when we require them, or on terms that are acceptable to us. If adequate funds are not available to us on a timely basis, we may be required to delay, limit, reduce or terminate our research and development efforts or other operations or activities that may be necessary to commercialize our product candidates.

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Most of our recent revenue has been earned from collaboration partners for our product candidates under development.

If either or both of our Astellas and AstraZeneca collaborations were to be terminated, we could require significant additional capital in order to proceed with development and commercialization of our product candidates, including with respect to our commercialization of roxadustat for the treatment of anemia caused by CKD, or we may require additional partnering in order to help fund such development and commercialization. If adequate funds or partners are not available to us on a timely basis or on favorable terms, we may be required to delay, limit, reduce or terminate our development or commercialization efforts or other operations.

We may encounter difficulties in managing our growth and expanding our operations successfully.

As we seek to advance our product candidates through clinical trials and commercialization, we will need to expand our development, regulatory, manufacturing, commercialization and administration capabilities or contract with third parties to provide these capabilities for us. As our operations expand and we continue to undertake the efforts and expense to operate as a public reporting company, we expect that we will need to increase the responsibilities on members of management in order to manage any future growth effectively. Our failure to accomplish any of these steps could prevent us from successfully implementing our strategy and maintaining the confidence of investors in us.

Loss of senior management and key personnel could adversely affect our business.

We are highly dependent on members of our senior management team, including Enrique Conterno, our Chief Executive Officer. The loss of the services of Mr. Conterno or any of our senior management could significantly impact the development and commercialization of our products and product candidates and our ability to successfully implement our business strategy.

Recruiting and retaining qualified commercial, development, scientific, clinical, and manufacturing personnel are and will continue to be critical to our success, particularly as we expand our commercialization operations. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize product candidates. We may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the intense competition among numerous biopharmaceutical companies for similar personnel.

There is also significant competition, in particular in the San Francisco Bay Area, for the hiring of experienced and qualified personnel, which increases the importance of retention of our existing personnel. If we are unable to continue to attract and retain personnel with the quality and experience applicable to our product candidates, our ability to pursue our strategy will be limited and our business and operations would be adversely affected.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may have to limit commercial operations.

We face an inherent risk of product liability as a result of the clinical testing, manufacturing and commercialization of our product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under state consumer protection acts. If we are unable to obtain insurance coverage at levels that are appropriate to maintain our business and operations, or if we are unable to successfully defend ourselves against product liability claims, we may incur substantial liabilities or otherwise cease operations. Product liability claims may result in:

- · termination of further development of unapproved product candidates or significantly reduced demand for any approved products;
- material costs and expenses to defend the related litigation;
- a diversion of time and resources across the entire organization, including our executive management;
- product recalls, withdrawals or labeling restrictions;
- termination of our collaboration relationships or disputes with our collaboration partners; and
- reputational damage negatively impacting our other product candidates in development.

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If we fail to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims, we may not be able to continue to develop our product candidates. We maintain product liability insurance in a customary amount for the stage of development of our product candidates. Although we believe that we have sufficient coverage based on the advice of our third-party advisors, there can be no assurance that such levels will be sufficient for our needs. Moreover, our insurance policies have various exclusions, and we may be in a dispute with our carrier as to the extent and nature of our coverage, including whether we are covered under the applicable product liability policy. If we are not able to ensure coverage or are required to pay substantial amounts to settle or otherwise contest the claims for product liability, our business and operations would be negatively affected.

Our business and operations would suffer in the event of computer system failures.

Despite the implementation of security measures, our internal computer systems, and those of our CROs, collaboration partners, and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, fire, terrorism, war and telecommunication and electrical failures. We upgraded our disaster and data recovery capabilities in 2019, and have continued to upgrade these capabilities. However, to the extent that any disruption or security breach, in particular with our partners' operations, results in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and it could result in a material disruption and delay of our drug development programs. For example, the loss of clinical trial data from completed, ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data.

We depend on sophisticated information technology systems and could face a cyber-attack or other breach of these systems.

We rely on information technology systems to process, transmit and store electronic information in our day-to-day operations. The size and complexity of our information technology systems makes them vulnerable to a cyber-attack, malicious intrusion, breakdown, destruction, loss of data privacy or other significant disruption. While we upgraded our disaster data recovery program in March 2019, a successful attack could result in the theft or destruction of intellectual property, data, or other misappropriation of assets, or otherwise compromise our confidential or proprietary information and disrupt our operations. Cyber-attacks are becoming more sophisticated and frequent. We have invested in our systems and the protection and recoverability of our data to reduce the risk of an intrusion or interruption, and we monitor and test our systems on an ongoing basis for any current or potential threats. There can be no assurance that these measures and efforts will prevent future interruptions or breakdowns. If we fail to maintain or protect our information technology systems and data integrity effectively or fail to anticipate, plan for or manage significant disruptions to these systems, we could have difficulty preventing, detecting and controlling such cyber-attacks and any such attacks could result in losses described above as well as disputes with physicians, patients and our partners, regulatory sanctions or penalties, increases in operating costs and expenses, expenses or lost revenues or other adverse consequences, any of which could have a material adverse effect on our business, results of operations, financial condition, prospects and cash flows.

Our headquarters are located near known earthquake fault zones.

We and some of the third-party service providers on which we depend for various support functions are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires, and has been affected by the COVID-19 pandemic, including economic disruption resulting from the related shelter-in-place and stay-at-home governmental orders.

After a comprehensive earthquake risk analysis conducted by Marsh Risk, we decided not to purchase earthquake or flood insurance. Based upon (among other factors) the Marsh Risk analysis, the design and construction of our building, the expected potential loss, and the costs and deductible associated with earthquake and flood insurance, we chose to self-insure. However, earthquakes or other natural disasters could severely disrupt our operations, or have a larger cost than expected, and have a material adverse effect on our business, results of operations, financial condition and prospects.

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If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, or otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place are unlikely to provide adequate protection in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business.

Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events, such as the COVID-19 pandemic. If such an event were to affect our supply chain, it could have a material adverse effect on our business.

Risks Related to Our Common Stock

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above your purchase price.

In general, pharmaceutical, biotechnology and other life sciences company stocks have been highly volatile in the current market. The volatility of pharmaceutical, biotechnology and other life sciences company stocks is sometimes unrelated to the operating performance of particular companies and biotechnology and life science companies stocks often respond to trends and perceptions rather than financial performance. In particular, the market price of shares of our common stock could be subject to wide fluctuations in response to the following factors:

- results of clinical trials of our product candidates, including roxadustat and pamrevlumab;
- the timing of the release of results of and regulatory updates regarding our clinical trials;
- the level of expenses related to any of our product candidates or clinical development programs;
- results of clinical trials of our competitors' products;
- safety issues with respect to our product candidates or our competitors' products;
- · regulatory actions with respect to our product candidates and any approved products or our competitors' products;
- fluctuations in our financial condition and operating results, which will be significantly affected by the manner in which we recognize revenue from the achievement of milestones under our collaboration agreements;
- adverse developments concerning our collaborations and our manufacturers;
- the termination of a collaboration or the inability to establish additional collaborations;
- the inability to obtain adequate product supply for any approved drug product or inability to do so at acceptable prices;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- changes in legislation or other regulatory developments affecting our product candidates or our industry;
- fluctuations in the valuation of the biotechnology industry and particular companies perceived by investors to be comparable to us;
- speculation in the press or investment community;
- announcements of investigations or regulatory scrutiny of our operations or lawsuits filed against us;
- activities of the government of China, including those related to the pharmaceutical industry as well as industrial policy generally;
- performance of other U.S. publicly traded companies with significant operations in China;
- changes in market conditions for biopharmaceutical stocks; and
- the other factors described in this "Risk Factors" section.

As a result of fluctuations caused by these and other factors, comparisons of our operating results across different periods may not be accurate indicators of our future performance. Any fluctuations that we report in the future may differ from the expectations of market analysts and investors, which could cause the price of our common stock to fluctuate significantly. Moreover, securities class action litigation has often been initiated against companies following periods of volatility in their stock price. This type of litigation could result in substantial costs and divert our management's attention and resources and could also require us to make substantial payments to satisfy judgments or to settle litigation.

Our principal stockholders own a significant percentage of our stock and will be able to exercise influence over stockholder approvals.

As of January 31, 2021, our executive officers, directors and principal stockholders, together with their respective affiliates, owned approximately 41.43% of our common stock, including shares subject to outstanding options that are exercisable within 60 days after such date and shares issuable upon settlement of restricted stock units that will vest within 60 days after such date. This percentage is based upon information supplied by officers, directors and principal stockholders and Schedules 13D and 13G, if any, filed with the SEC, which information may not be accurate as of January 31, 2020. Accordingly, these stockholders will be able to exert a significant degree of influence over our management and affairs and over matters requiring stockholder approval, including the election of our board of directors and approval of significant corporate transactions. The interests of this group may differ from those of other stockholders and they may vote their shares in a way that is contrary to the way other stockholders vote their shares. This concentration of ownership could have the effect of entrenching our management and/or the board of directors, delaying or preventing a change in our control or otherwise discouraging a potential acquirer from attempting to obtain control of us, which in turn could have a material and adverse effect on the fair market value of our common stock.

We may engage in acquisitions that could dilute stockholders and harm our business.

We may, in the future, make acquisitions of or investments in companies that we believe have products or capabilities that are a strategic or commercial fit with our present or future product candidates and business or otherwise offer opportunities for us. In connection with these acquisitions or investments, we may:

- issue stock that would dilute our existing stockholders' percentage of ownership;
- incur debt and assume liabilities; and
- · incur amortization expenses related to intangible assets or incur large and immediate write-offs.

We may not be able to complete acquisitions on favorable terms, if at all. If we do complete an acquisition, we cannot assure you that it will ultimately strengthen our competitive position or that it will be viewed positively by customers, financial markets or investors. Furthermore, future acquisitions could pose numerous additional risks to our operations, including:

- problems integrating the purchased business, products or technologies, or employees or other assets of the acquisition target;
- increases to our expenses;
- disclosed or undisclosed liabilities of the acquired asset or company;
- diversion of management's attention from their day-to-day responsibilities;
- · reprioritization of our development programs and even cessation of development and commercialization of our current product candidates;
- · harm to our operating results or financial condition;
- entrance into markets in which we have limited or no prior experience; and
- potential loss of key employees, particularly those of the acquired entity.

We may not be able to complete any acquisitions or effectively integrate the operations, products or personnel gained through any such acquisition.

Provisions in our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, and may prevent attempts by our stockholders to replace or remove our current directors or management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws contain provisions that may have the effect of discouraging, delaying or preventing a change in control of us or changes in our management. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors pursuant to a resolution adopted by a majority of the total number of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed prior to the end of their term only for cause;
- · provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- · require a supermajority vote of the holders of our common stock or the majority vote of our board of directors to amend our bylaws; and
- require a supermajority vote of the holders of our common stock to amend the classification of our board of directors into three classes and to amend certain other provisions of our certificate of incorporation.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

Moreover, because we are incorporated in Delaware, we are governed by certain anti-takeover provisions under Delaware law which may discourage, delay or prevent someone from acquiring us or merging with us whether or not it is desired by or beneficial to our stockholders. We are subject to the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Any provision of our amended and restated certificate of incorporation, our amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Changes in our tax provision or exposure to additional tax liabilities could adversely affect our earnings and financial condition.

As a multinational corporation, we are subject to income taxes in the U.S. and various foreign jurisdictions. Significant judgment is required in determining our global provision for income taxes and other tax liabilities. In the ordinary course of a global business, there are intercompany transactions and calculations where the ultimate tax determination is uncertain. Our income tax returns are subject to audits by tax authorities. Although we regularly assess the likelihood of adverse outcomes resulting from these examinations to determine our tax estimates, a final determination of tax audits or tax disputes could have an adverse effect on our results of operations and financial condition.

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We are also subject to non-income taxes, such as payroll, excise, customs and duties, sales, use, value-added, net worth, property, gross receipts, and goods and services taxes in the U.S., state and local, and various foreign jurisdictions. We are subject to audit and assessments by tax authorities with respect to these non-income taxes and may have exposure to additional non-income tax liabilities, which could have an adverse effect on our results of operations and financial condition.

Federal and state tax laws impose substantial restrictions on the utilization of net operating loss and credit carryforwards in the event of an "ownership change" for tax purposes, as defined in IRC Section 382. If additional ownership change occurs, the utilization of net operating loss and credit carryforwards could be significantly reduced.

In addition, our judgment in providing for the possible impact of the Tax Act remains subject to developing interpretations of the provisions of the Tax Act. As regulations and guidance evolve with respect to the Tax Act, we continue to examine the impact to our tax provision or exposure to additional tax liabilities, which could have a material adverse effect on our business, results of operations or financial condition.

Tariffs imposed by the U.S. and those imposed in response by other countries could have a material adverse effect on our business.

Changes in U.S. and foreign governments' trade policies have resulted in, and may continue to result in, tariffs on imports into and exports from the U.S. Throughout 2018 and 2019, the U.S. imposed tariffs on imports from several countries, including China. In response, China has proposed and implemented their own tariffs on certain products, which may impact our supply chain and our costs of doing business. If we are impacted by the changing trade relations between the U.S. and China, our business and results of operations may be negatively impacted. Continued diminished trade relations between the U.S. and other countries, including potential reductions in trade with China and others, as well as the continued escalation of tariffs, could have a material adverse effect on our financial performance and results of operations.

Our certificate of incorporation designates courts located in Delaware as the sole forum for certain proceedings, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state and federal courts located in the State of Delaware will be the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law: (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated by-laws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. This provision would not apply to suits brought to enforce a duty or liability created by the Exchange Act. Furthermore, Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all such Securities Act actions. Accordingly, both state and federal courts have jurisdiction to entertain such claims. To prevent having to litigate claims in multiple jurisdictions and the threat of inconsistent or contrary rulings by different courts, among other considerations, our amended and restated certificate of incorporation further provides that the U.S. federal district courts will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act. While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated certificate of incorporation. This may require significant additional costs associated with resolving such action in other juri

This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. If a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

We do not plan to pay dividends. Capital appreciation will be your sole possible source of gain, which may never occur.

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future and investors seeking cash dividends should not purchase our common stock. We plan to retain any earnings to invest in our product candidates and maintain and expand our operations. Therefore, capital appreciation, or an increase in your stock price, which may never occur, may be the only way to realize any return on your investment.

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ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our corporate and research and development operations are located in San Francisco, California, where we lease approximately 234,000 square feet of office and laboratory space with approximately 35,000 square feet subleased. The lease for our San Francisco headquarters expires in 2023. We also lease approximately 67,000 square feet of office and manufacturing space in Beijing, China, and multiple office spaces in Beijing and Shanghai, China. Our leases in China expire in 2023. We have constructed a commercial manufacturing facility of approximately 5,500 square meters in Cangzhou, China, on approximately 33,000 square meters of land. Our right to use such land expires in 2068. We believe our facilities are adequate for our current needs and that suitable additional or substitute space would be available if needed.

ITEM 3. LEGAL PROCEEEDINGS

We are a party to various legal actions that arose in the ordinary course of our business. We recognize accruals for any legal action when we conclude that a loss is probable and reasonably estimable. We did not have any material accruals for any currently active legal action in our consolidated balance sheets as of December 31, 2020, as we could not predict the ultimate outcome of these matters, or reasonably estimate the potential exposure.

On April 20, 2020, in response to an invalidation action brought against certain FibroGen United Kingdom patents by Akebia, the United Kingdom court handed down a decision invalidating United Kingdom designations of European Patent Nos. 1463823, 1633333, 2298301, 2322153, and 2322155. The United Kingdom designation to European Patent No. 2289531 was held to be valid in amended form, but not infringed by Akebia. We and our partner Astellas have filed an appeal of the decision in the United Kingdom Court of Appeal.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information for Common Stock

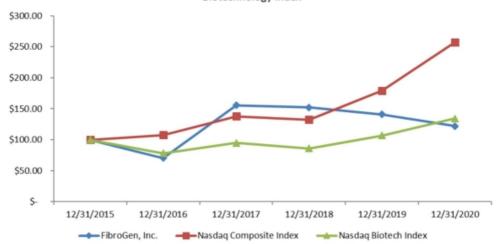
Our common stock has been listed on the NASDAQ Global Select Market ("NASDAQ") since November 14, 2014, under the symbol "FGEN." Prior to our initial public offering, there was no public market for our common stock.

Stock Price Performance Graph

The following graph illustrates a comparison of the total cumulative stockholder return for our common stock since December 31, 2015 to two indices: the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The graph assumes an initial investment of \$100 on December 31, 2015, in our common stock, the stocks comprising the NASDAQ Composite Index, and the stocks comprising the NASDAQ Biotechnology Index. The stockholder return shown in the graph below is not necessarily indicative of future performance, and we do not make or endorse any predictions as to future stockholder returns.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN

Among FibroGen, Inc., the NASDAQ Composite Index and the NASDAQ Biotechnology Index



The above Stock Price Performance Graph and related information shall not be deemed "soliciting material" or to be "filed" with the Securities and Exchange Commission, nor shall such information be incorporated by reference into any future filing under the Securities Act or Exchange Act, except to the extent that we specifically incorporate it by reference into such filing.

Dividend Policy

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

Stockholders

As of January 31, 2021, there were 129 registered stockholders of record for our common stock. This number of registered stockholders does not include stockholders whose shares are held in street name by brokers and other nominees, or may be held in trust by other entities. Therefore, the actual number of stockholders is greater than this number of registered stockholders of record.

Use of Proceeds from Initial Public Offering of Common Stock

On November 13, 2014, our Registration Statement on Form S-1, as amended (Reg. Nos. 333-199069 and 333-200189) was declared effective in connection with the initial public offering of our common stock. There has been no material change in the planned use of proceeds from our initial public offering as described in our final prospectus filed with the SEC pursuant to Rule 424(b) under the Securities Act on November 14, 2014.

Recent Sales of Unregistered Securities

None.

Purchases of Equity Securities by the Issuer and Affiliated Purchasers

None.

ITEM 6. SELECTED FINANCIAL DATA

We have adopted the amendment to eliminate Item 301 of Regulation S-K, and we are omitting this disclosure in reliance thereon.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes and other financial information included in Item 8 of this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report, including information with respect to our plans and strategy for our business, international operations and product candidates, includes forward-looking statements that involve risks and uncertainties. You should review the "Risk Factors" section of this Annual Report for a discussion of important factors that could cause our actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

BUSINESS OVERVIEW

We are headquartered in San Francisco, California, with subsidiary offices in Beijing and Shanghai, People's Republic of China ("China"). We are a leading biopharmaceutical company developing and commercializing a pipeline of first-in-class therapeutics. We apply our pioneering expertise in hypoxia-inducible factor ("HIF") biology, 2-oxoglutarate enzymology, connective tissue growth factor ("CTGF") biology, and clinical development to advance innovative medicines for the treatment of anemia, fibrotic disease, and cancer.

Roxadustat, our most advanced product, is an oral small molecule inhibitor of HIF prolyl hydroxylase (together with HIF, "HIF-PH") activity that has received marketing authorization in China (tradename: 爱瑞卓®) for the treatment of anemia caused by chronic kidney disease ("CKD") in dialysis and non-dialysis patients. EVRENZO® (roxadustat) is also approved in Japan and Chile for the treatment of anemia associated with CKD in dialysis and non-dialysis patients.

Our New Drug Application ("NDA") filing in the United States ("U.S.") for roxadustat for the treatment of anemia in dialysis and non-dialysis CKD patients was submitted for review in December 2019 to the U.S. Food and Drug Administration ("FDA") and in December 2020, the FDA extended the review period of the NDA by three months for FibroGen to submit additional analyses of existing roxadustat clinical data, and set a new Prescription Drug User Fee Act ("PDUFA") goal date of March 20, 2021. On March 1, 2021, the FDA informed us that the Cardiovascular and Renal Drugs Advisory Committee will hold an advisory committee meeting to review the NDA for roxadustat. The date of the advisory committee meeting has not been set. As a result of this communication, we will not receive an approval decision by the PDUFA goal date. In Europe, the Marketing Authorization Application ("MAA") filing for roxadustat for the treatment of anemia in dialysis and non-dialysis CKD patients was accepted for regulatory review by the European Medicines Agency ("EMA") in May 2020 and Astellas Pharma Inc. ("Astellas") expects an approval decision mid-2021.

Roxadustat is in Phase 3 clinical development in the U.S. and Europe and in Phase 2/3 development in China for anemia associated with myelodysplastic syndromes. Roxadustat is in Phase 2 clinical development for chemotherapy-induced anemia.

Pamrevlumab, an anti-CTGF human monoclonal antibody, is in Phase 3 clinical development for the treatment of idiopathic pulmonary fibrosis ("IPF"), pancreatic cancer and Duchenne muscular dystrophy.

Impact of COVID-19

On March 11, 2020, COVID-19, a disease caused by a novel strain of the coronavirus, was characterized as a pandemic by the World Health Organization. The rapid spread has resulted in authorities implementing numerous measures to contain the virus, such as travel restrictions, social distancing requirements, quarantines, shelter-in-place orders or voluntarily adopted practices, and business shutdowns.

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We have taken measures to minimize the health risks of COVID-19 to our staff, patients, healthcare providers and their communities, as their safety and well-being are our top priority. In the U.S., our employees are working remotely when possible, while in China they have returned to work in our offices, manufacturing plants, and are performing medical affairs out in the field. While we have seen some impacts from COVID-19, such as slower enrollment in our clinical trials, particularly our Phase 3 IPF program, we do not know if, or to what extent, these effects will continue in the future, as the impact of the COVID-19 pandemic continues to unfold. The effect on our operational and financial performance beyond those effects described above, including any impact on sales of roxadustat, will depend in large part on future developments with the pandemic, which cannot be predicted with confidence at this time. Future developments include the duration, scope, and severity of the COVID-19 pandemic, the actions taken to contain or mitigate its impact, the impact on governmental programs and budgets, the impact on healthcare systems and operating procedures, the development of treatments or vaccines, and the resumption of widespread economic activity. Due to the inherent uncertainty of the largely unprecedented and rapidly evolving situation, we are unable to predict with any confidence the likely impact of the COVID-19 pandemic on our future operations.

The financial results for the year ended December 31, 2020 were not significantly impacted by COVID-19 relative to prior years. However, we will continue to monitor, and to the extent possible, mitigate the impact of the COVID-19 pandemic on our business.

Financial Highlights

	Years Ended December 31,							
		2020		2019	2018			
		(in th	ousa)				
Result of Operations								
Revenue	\$	176,319	\$	256,577	\$	212,958		
Operating costs and expenses		368,199		345,891		299,651		
Net loss		(189,291)		(76,970)		(86,420)		
Net loss per share - basic and diluted	\$	(2.11)	\$	(0.89)	\$	(1.03)		
				December 31, 2020		December 31, 2019		
				(in thou	is)			
Balance Sheet								
Cash and cash equivalents			\$	678,393	\$	126,266		
Short-term and long-term investments			\$	8,388	\$	468,609		
Accounts receivable			\$	41,883	\$	28,455		

Our revenue for the year ended December 31, 2020 included the revenues recognized related to the following:

- \$15.0 million regulatory milestone associated with the NDA approval in Japan;
- \$80.6 million development revenue recognized under collaboration agreements with our partners Astellas and AstraZeneca AB
 ("AstraZeneca");
- \$72.5 million of net product revenue from roxadustat commercial sales in China; and
- \$8.9 million of drug product revenue related to roxadustat bulk drug or active pharmaceutical ingredient ("API") deliveries to AstraZeneca and Astellas.

As comparison, our revenue for the year ended December 31, 2019 included the revenues recognized related to the following:

- \$130.0 million total of two regulatory milestones associated with the planned MAA submission to the EMA under the collaboration agreement
 with Astellas for roxadustat as a treatment for dialysis and non-dialysis CKD patients;
- \$50.0 million regulatory milestone associated with the NDA submission to the FDA under the collaboration agreement with AstraZeneca for roxadustat as a treatment for dialysis and non-dialysis CKD patients;
- \$22.0 million total of three regulatory milestones associated with roxadustat being included on the updated National Reimbursement Drug List ("NRDL") released by China's National Healthcare Security Administration ("NHSA");
- \$12.5 million regulatory milestone associated with the NDA approval in Japan; and
- \$36.3 million reduction in drug product revenue of a change in estimated variable consideration related to the API product revenue that was
 recognized in 2018, which reflected the total difference between estimated and actual listed price and yield from the manufacture of bulk
 product tablets.

Operating costs and expenses increased for the year ended December 31, 2020 compared to the prior year primarily due to the following:

- · Higher clinical trial expenses associated with post-approval safety studies in China, and commencement of Phase 3 trials for pamrevlumab;
- Higher drug development expenses associated with drug substance manufacturing activities related to pamrevlumab, partially offset by lower
 activities related to roxadustat and capitalization of inventory manufacturing costs;
- · Higher employee-related expenses primarily resulting from higher average compensation level and headcount;
- · Higher stock-based compensation expense, primarily due to the cumulative impact of stock option grant activities;
- Higher legal expenses primarily associated with patent-related activities in the United Kingdom;
- Lower sales and marketing expenses due to a reversal in co-promotion expenses with AstraZeneca as a result of the China Amendment between FibroGen China and AstraZeneca; and
- · Lower outside services due to lower consulting expenses and scientific contract work related to roxadustat Phase 3 and submission activities.

Our research and development expenses were \$252.9 million, \$209.3 million and \$235.8 million for the years ended December 31, 2020, 2019 and 2018, respectively. Since inception and through December 31, 2020, we have incurred a total of approximately \$2.2 billion in research and development expenses, a majority of which relates to the development of roxadustat, pamrevlumab and other HIF-PH inhibitors. We expect to continue to incur significant expenses and operating losses over at least the next several years and we expect our research and development expenses to increase in the future as we advance our product candidates through clinical trials and expand our product candidate portfolio. In addition, we expect to incur significant expenses relating to seeking regulatory approval for our product candidates and commercializing those products in various markets, including China. We consider the active management and development of our clinical pipeline to be particularly crucial to our long-term success. The process of conducting the necessary clinical research to obtain regulatory approval is costly and time consuming.

The actual probability of success for each of our product candidates and clinical programs, and our ability to generate product revenue and become profitable, depends upon a variety of factors, including the quality of the product candidate, clinical results, investment in the program, competition, manufacturing capability, commercial viability, and our and our partners' ability to successfully execute our development and commercialization plans. For a description of the numerous risks and uncertainties associated with product development, refer to "Risk Factors."

During the year ended December 31, 2020, we had a net loss of \$189.3 million, or net loss per basic and diluted share of \$2.11, as compared to a net loss of \$77.0 million, or net loss per basic and diluted share of \$0.89 for the prior year, primarily due to a decrease in revenue and an increase in operating expenses.

Cash and cash equivalents, investments and accounts receivable totaled \$728.7 million at December 31, 2020, an increase of \$105.4 million from December 31, 2019, primarily due to cash provided by operations.

Collaboration Partnerships for Roxadustat

Our current and future research, development, manufacturing and commercialization efforts with respect to roxadustat and our other product candidates currently in development depend on funds from our collaboration agreements with Astellas and AstraZeneca as described below.

Astellas

In June 2005, we entered into a collaboration agreement with Astellas for the development and commercialization (but not manufacture) of roxadustat for the treatment of anemia in Japan ("Japan Agreement"). In April 2006, we entered into the Europe Agreement with Astellas for roxadustat for the treatment of anemia in Europe, the Commonwealth of Independent States, the Middle East, and South Africa. Under these agreements, we provide Astellas the right to develop and commercialize roxadustat for anemia indications in these territories.

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We share responsibility with Astellas for clinical development activities required for the U.S. and the Europe regulatory approval of roxadustat, and share equally those development costs under the agreed development plan for such activities. Astellas will be responsible for clinical development activities and all associated costs required for regulatory approval in all other countries in the Astellas territories. Astellas will own and have responsibility for regulatory filings in its territories. We are responsible, either directly or through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the agreements. Astellas is responsible for roxadustat commercialization activities in the Astellas territories.

The Astellas agreements will continue in effect until terminated. Either party may terminate the agreements for certain material breaches by the other party. In addition, Astellas will have the right to terminate the agreements for certain specified technical product failures, upon generic sales reaching a particular threshold, upon certain regulatory actions, or upon our entering into a settlement admitting the invalidity or unenforceability of our licensed patents. Astellas may also terminate the agreements for convenience upon advance written notice to us. In the event of any termination of the agreements, Astellas will transfer and assign to us the regulatory filings for roxadustat and will assign or license to us the relevant trademarks used with the products in the Astellas territories. Under certain terminations, Astellas is also obligated to pay us a termination fee.

Consideration under these agreements includes a total of \$360.1 million in upfront and non-contingent payments, and milestone payments totaling \$557.5 million, of which \$542.5 million are development and regulatory milestones and \$15.0 million are commercial-based milestones. Total consideration, excluding development cost reimbursement and product sales-related payments, could reach \$917.6 million. The aggregate amount of such consideration received through December 31, 2020 totals \$645.1 million.

Additionally, under these agreements, Astellas pays 100% of the commercialization costs in their territories. In Europe, Astellas will pay us a tiered transfer price for our manufacture and supply of roxadustat based on net sales of roxadustat in the low 20% range. In Japan, Astellas pays us a transfer price in the low 20% range of the list price published by the Japanese Ministry of Health, Labour and Welfare, adjusted for certain elements.

During the fourth quarter of 2020, the Japanese Ministry of Health, Labour and Welfare approved EVRENZO® (roxadustat) for the treatment of anemia of CKD in adult patients not on dialysis. Accordingly, the consideration of \$15.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the Japan Agreement in the fourth quarter of 2020, substantially all of which was recognized as revenue during the year ended December 31, 2020 from performance obligations satisfied or partially satisfied.

In September 2019, the Japanese Ministry of Health, Labour and Welfare approved roxadustat for the treatment of anemia associated with dialysis CKD patients. Accordingly, the consideration of \$12.5 million associated with this milestone was included in the transaction price and allocated to performance obligations under the Japan Agreement in the third quarter of 2019. This milestone payment was received in October 2019.

During the second quarter of 2019, we received positive topline results from analyses of pooled major adverse cardiovascular event ("MACE") and MACE+ data from its Phase 3 trials evaluating roxadustat as a treatment for dialysis and non-dialysis CKD patients, enabling Astellas to prepare for an MAA submission to the EMA in the second quarter of 2020, following our NDA submission to the FDA in 2019 and acceptance for review in February 2020. These milestones became probable of being achieved in the second quarter of 2019, and substantially all of the total consideration of \$130.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the Europe Agreement in the second quarter of 2019, of which \$128.8 million was recognized as revenue during 2019, and \$0.8 million was recognized as revenue during 2020, from performance obligations satisfied or partially satisfied. According to the Europe Agreement, these milestone payments were billed to Astellas upon the submission of an MAA in the second quarter of 2020 and the total \$130.0 million was received during the same quarter.

In 2018, FibroGen and Astellas entered into an amendment to the Japan Agreement that will allow Astellas to manufacture roxadustat drug product for commercialization in Japan (the "Japan Amendment"). Under this amendment, FibroGen would continue to manufacture and supply roxadustat API to Astellas. The commercial terms of the Japan Agreement relating to the transfer price for roxadustat for commercial use remain substantially the same, reflecting an adjustment for the manufacture of drug product by Astellas rather than FibroGen. We fulfilled delivery of a total of \$64.8 million API under this amendment in 2018. In 2019, a change in estimated variable consideration resulted in a \$36.3 million reduction to revenue associated with these API shipments, at the time the listed price for roxadustat was issued by the Japanese Ministry of Health, Labour and Welfare, which reflected the total difference between estimated and actual listed price and yield from the manufacture of bulk product tablets. In addition, in 2020, we recorded another \$4.0 million reduction to revenue associated with these API shipments, related to a change in estimated variable consideration, based on the API held by Astellas at March 31, 2020 adjusted to reflect the updated listed price for roxadustat issued by the Japanese Ministry of Health, Labour and Welfare and possible future changes to the listed price, adjusted for the timing of and estimated bulk product strength mix intended to be manufactured by Astellas, estimated cost to convert the API to bulk product tablets, and estimated yield from the manufacture of bulk product tablets, among others.

During the second quarter of 2020, we fulfilled delivery obligations under the term of the Japan Amendment, and recognized related drug product revenue of \$8.2 million in the same period. The amount represents variable consideration and was estimated based on the quantity of product shipped, actual listed price for roxadustat issued by the Japanese Ministry of Health, Labour and Welfare and possible future changes to the listed price, adjusted for the timing of and estimated bulk product strength mix intended to be manufactured by Astellas, estimated cost to convert the API to bulk product tablets, and estimated yield from the manufacture of bulk product tablets, among others.

During the fourth quarter of 2020, we shipped bulk drug product from process validation supplies for commercial sales under the term of the Europe Agreement. We constrained the estimated variable consideration due to a high degree of uncertainty associated to the final consideration because of an extended length of time over which the considerations may be adjusted. As a result, we constrained the consideration from this shipment, and recorded \$1.4 million as current deferred revenue and \$4.6 million as long-term deferred revenue as of December 31, 2020. The deferred revenue will be recognized over the duration of the contract and when uncertainty is resolved.

In the fourth quarter of 2018, we were engaged in the final stages of review with our partners over the proposed development of roxadustat for the treatment of chemotherapy-induced anemia. AstraZeneca and Astellas approved the program in December 2018 and January 2019, respectively. Costs associated with the development of this indication are shared 50-50 between our two partners. For revenue recognition purposes, we concluded that this new indication represents a modification to the Europe agreements and will be accounted for separately, meaning the development costs associated with the new indications are distinct from the original development costs. The development service period for roxadustat for the treatment of CIA under the Europe Agreement is estimated to continue through the end of 2023 to allow for development of this indication.

In addition, as of December 31, 2020, Astellas had separate investments of \$80.5 million in the equity of FibroGen, Inc.

AstraZeneca

In July 2013, we entered into the U.S./RoW Agreement a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in the U.S. and all territories not previously licensed to Astellas, except China. In July 2013, through our China subsidiary and related affiliates, we entered into the China Agreement a collaboration agreement with AstraZeneca for roxadustat for the treatment of anemia in China. Under these agreements, we provide AstraZeneca the right to develop and commercialize roxadustat for anemia in these territories. We share responsibility with AstraZeneca for clinical development activities required for U.S. regulatory approval of roxadustat, and FibroGen will transfer the U.S. NDA to AstraZeneca upon approval. AstraZeneca will hold the equivalent regulatory filings in the other licensed countries.

In 2015, we reached the \$116.5 million cap on our initial funding obligations (during which time we shared 50% of the joint initial development costs), therefore all development and commercialization costs for roxadustat for the treatment of anemia in CKD in the U.S., Europe, Japan and all other markets outside of China have been paid by Astellas and AstraZeneca since reaching the cap.

In China, FibroGen (China) Medical Technology Development Co., Ltd. ("FibroGen Beijing") will conduct the development work for CKD anemia, will hold all of the regulatory licenses issued by China regulatory authorities, and will be primarily responsible for regulatory, clinical and manufacturing. China development costs are shared 50/50. AstraZeneca is also responsible for 100% of development expenses in all other licensed territories outside of China. Outside of China, we are responsible, through our contract manufacturers, for the manufacture and supply of all quantities of roxadustat to be used in development and commercialization under the AstraZeneca agreements.

Under the AstraZeneca agreements, we will receive upfront and subsequent non-contingent payments totaling \$402.2 million. Potential milestone payments under the agreements total \$1.2 billion, of which \$571.0 million are development and regulatory milestones and \$652.5 million are commercial-based milestones. Total consideration under the agreements, excluding development cost reimbursement, transfer price payments, royalties and profit share, could reach \$1.6 billion. The aggregate amount of such consideration received through December 31, 2020 totals \$516.2 million.

Under the U.S./RoW Agreement, AstraZeneca will pay for all commercialization costs in the U.S. and RoW and AstraZeneca will be responsible for the U.S. commercialization of roxadustat, with FibroGen undertaking specified commercial activities in the U.S. In addition, we will receive a transfer price for delivery of commercial product based on a percentage of net sales in the low- to mid-single digit range and AstraZeneca will pay us a tiered royalty on net sales of roxadustat in the low 20% range.

Under the China Agreement, which is conducted through FibroGen China Anemia Holdings, Ltd. ("FibroGen Cayman"), FibroGen Beijing, and FibroGen International (Hong Kong) Limited (collectively, ("FibroGen China, the commercial collaboration was structured as a 50/50 profit share, which was amended by the China Amendment in the third quarter of 2020, as discussed and defined below in *China Amendment*.

AstraZeneca may terminate the U.S./RoW Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon 180 days prior written notice at will. If AstraZeneca terminates the U.S./RoW Agreement at will, in addition to any unpaid non-contingent payments, it will be responsible for paying for a substantial portion of the post-termination development costs under the agreed development plan until regulatory approval.

AstraZeneca may terminate the China Agreement upon specified events, including our bankruptcy or insolvency, our uncured material breach, technical product failure, or upon advance prior written notice at will. If AstraZeneca terminates our China Agreement at will, it will be responsible for paying for transition costs as well as make a specified payment to FibroGen.

In the event of any termination of the agreements, but subject to modification upon termination for technical product failure, AstraZeneca will transfer and assign to us any regulatory filings and approvals for roxadustat in the affected territories that they may hold under our agreements, grant us licenses and conduct certain transition activities.

As mentioned above, during the second quarter of 2019, we received positive topline results from analyses of pooled MACE and MACE+ data from its Phase 3 trials for roxadustat, enabling our U.S. NDA submission to the FDA. The regulatory milestone payment associated with this NDA submission became probable of being achieved in the second quarter of 2019. Accordingly, the consideration of \$50.0 million associated with this milestone was included in the transaction price and allocated to performance obligations under the combined arrangement in the second quarter of 2019, of which \$42.4 million was recognized as revenue during 2019, and \$0.6 million was recognized as revenue during 2020, from performance obligations satisfied or partially satisfied. We submitted such NDA to the FDA in December 2019, which was accepted for review in February 2020. According to the U.S/RoW Agreement, this milestone payment is billable to AstraZeneca when the NDA is accepted by the FDA. Therefore, this \$50.0 million milestone was billed during the first quarter of 2020, the payment of which was fully received in April 2020.

In December 2019, roxadustat has been included on the updated NRDL released by China's NHSA for the treatment of anemia in CKD, covering patients who are non-dialysis-dependent as well as those who are dialysis-dependent. Accordingly, the total consideration of \$22.0 million associated with these milestones was included in the transaction price and allocated to performance obligations under the combined arrangement in the fourth quarter of 2019. This milestone payment was fully received during the first quarter of 2020.

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As mentioned above, in the fourth quarter of 2018, we were engaged in the final stages of review with our partners over the proposed development of roxadustat for the treatment of CIA. AstraZeneca and Astellas approved the program in December 2018 and January 2019, respectively. Costs associated with the development of this indication are expected to be shared 50-50 between our two partners. In addition to CIA, in December 2018, anemia of chronic inflammation and multiple myeloma have been approved for development by AstraZeneca and is expected to be fully funded by them. For revenue recognition purposes, we concluded that the approval of additional research and development services for these new indications represent modifications to our collaboration agreements in the periods in which approval was received. The research and development services associated with the new indications are distinct from other promises in our collaboration agreements, and will be accounted for separately. The development service period for roxadustat for the treatment of CIA, anemia of chronic inflammation and multiple myeloma under the AstraZeneca agreements is estimated to continue through the end of 2024, to allow for development of these additional indications.

China Amendment

On July 8, 2020, FibroGen China and AstraZeneca (together with FibroGen China, the "Parties") entered into an amendment, effective July 1, 2020, to the China Agreement, relating to the development and commercialization of roxadustat in China (the "China Amendment"). While the responsibilities of the Parties under the China Agreement remain largely the same, certain changes were made.

The China Amendment provides for the establishment of a jointly owned entity that will perform roxadustat distribution, as well as conduct sales and marketing through AstraZeneca. To prepare for the establishment of this jointly owned entity, in July 2020, FibroGen Beijing acquired Beijing Kangda Yongfu Pharmaceutical Co., LTD ("Kangda"). The purpose of the acquisition was to acquire a distribution license owned by Kangda for commercializing and distributing roxadustat in China. FibroGen Beijing continues to hold all of the regulatory licenses issued by China regulatory authorities and continues to be primarily responsible for regulatory, clinical, manufacturing, medical affairs and pharmacovigilance activities. In September 2020, FibroGen Beijing and AstraZeneca entered into an equity transfer agreement and shareholders agreement related to Kangda. Concurrently with the equity transfer, the two parties renamed Kangda to Beijing Falikang Pharmaceutical Co. Ltd. ("Falikang"). See Note 3, *Acquisition and Variable Interest Entity*, to the consolidated financial statements for details.

As Falikang is a distribution entity for roxadustat and AstraZeneca is the final decision maker for all the roxadustat commercialization activities, we lack the power criterion while AstraZeneca meets both the power and economic criteria under ASC 810, to direct the activities of Falikang that most significantly impact its performance. Therefore, we are not the primary beneficiary of Falikang. As a result, we accounted for our investment in Falikang under the equity method, and Falikang is not consolidated into our consolidated financial statements. In addition, we recognized our proportionate share of the reported profits or losses of Falikang, as other income (loss) in the consolidated statement of operations, and as an adjustment to its investment in unconsolidated subsidiary in the consolidated balance sheet. Falikang has not incurred material profit or loss to date.

In accordance with the China Amendment, we are currently in the interim period. The interim period is defined as the period from April 1, 2020 to the time when Falikang is fully operational, which commenced in January 2021. During the interim period, FibroGen continues to sell product directly to the distributors, who remain as our customers. The calculation for profit or loss share has changed related to sales of roxadustat in China for the period from April 1, 2020 onwards. With effect from April 1, 2020, the Parties have changed the method under which commercial expenses incurred by AstraZeneca are calculated and billed. AstraZeneca's co-promotion expenses for their sales and marketing efforts are now subject to a cap of a percentage of net sales. Once AstraZeneca has been fully reimbursed for their sales and marketing costs under the cap, AstraZeneca will bill the co-promotion expenses based on actual costs on a prospective basis. In addition, the China Amendment has allowed for a higher cost of manufacturing incurred by FibroGen Beijing to be included in the profit or loss share calculation, subject to an annual cap, among other changes.

Once Falikang is fully operational, AstraZeneca will bill the co-promotion expenses to Falikang, rather than FibroGen Beijing. In addition, FibroGen Beijing will manufacture and supply commercial product to Falikang based on an agreed upon transfer price. Development costs will continue to be shared 50/50 between the Parties.

As a result, the interim period primarily includes the following activities:

- Co-promotion expenses: The China Amendment revised the payment arrangements and calculation of the historical unpaid co-promotion expenses to AstraZeneca for its sales and marketing efforts associated with the commercial sales for roxadustat in China since the product launch. Under the previous China Agreement, payment of these historical co-promotion expenses was subject to certain profitability and cash flow thresholds. No amount of the historical co-promotion costs had been paid prior to the China Amendment as these thresholds had not yet been met. Under the China Amendment, a portion of the historical unpaid co-promotion expenses was adjusted to reduce the amount owed by FibroGen Beijing and the current period co-promotion expenses are capped at a percentage of net roxadustat sales in China. As a result, in the third quarter of 2020, we reversed approximately \$84.4 million of previously accrued co-promotion expenses payable, which was recorded as a reduction to selling, general and administrative expenses, where these expenses were initially recorded during the periods from the initiation of commercial activities in the first quarter of 2019 to the second quarter of 2020. The co-promotion expenses for the year ended December 31, 2020, capped at a percentage of net roxadustat sales in China, were \$27.2 million, included in the selling, general and administrative expenses. After this adjustment, as of December 31, 2020, \$16.9 million and \$11.5 million of the recalculated accrued co-promotion expenses were recorded in accounts payable and accrued liabilities, respectively, as they were anticipated to be paid within the next 12 months; and \$27.4 million of the recalculated accrued co-promotion expenses remained in the long-term liabilities, as it is not anticipated to be paid within the next 12 months.
- Profit share: Profit/loss share between FibroGen Beijing and AstraZeneca is based on a calculation of the current period net roxadustat sales in China and deductible expenses pursuant to the China Agreement. Based on the calculation revised under the China Amendment, profit was achieved during the third and fourth quarter of 2020. As a result, we recorded a profit share liability of \$7.0 million to AstraZeneca as of December 31, 2020 in the accrued and other current liabilities, which correspondingly reduced the deferred revenue related to the performance obligation in accordance with the China Agreement.

FibroGen, Inc. and AstraZeneca concurrently amended the U.S./RoW Agreement to reflect minor changes in the governance structure under the China Agreement.

Starting in the first quarter of 2021, our revenue will be made of 1) a transfer price from our sales to Falikang, and 2) sales made directly by FibroGen Beijing to distributors who have not transitioned to Falikang. The transfer price earned is expected to be in the range of 30-45% of Falikang's net sales, which reflects the fact that Falikang will pay AstraZeneca the commercialization expenses and AstraZeneca's profit share. For revenue recognition purposes, we estimate the total consideration on a per unit basis and recognize as we transfer control of the commercial drug product to Falikang.

Additional Information Related to Collaboration Agreements

Of the \$1.1 billion in development and regulatory milestones payable in the aggregate under our Astellas and AstraZeneca collaboration agreements, \$425.0 million is payable upon achievement of milestones relating to the submission and approval of roxadustat in dialysis-dependent CKD and non-dialysis-dependent CKD in the U.S. and Europe.

For more detailed discussions on the accounting for these agreements, refer to Note 4, Collaboration Agreements and Revenues, to the consolidated financial statements.

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Total cash consideration received through December 31, 2020 and potential cash consideration, other than development cost reimbursement, transfer price payments, royalties and profit share, pursuant to our existing collaboration agreements are as follows:

	Cash Received Through December 31, 2020		Additional Potential <u>Cash Payments</u> (in thousands)		Total Potential Cash Payments	
Astellasrelated-party:						
Japan Agreement	\$	105,093	\$	67,500	\$	172,593
Europe Agreement		540,000		205,000		745,000
Total Astellas		645,093		272,500		917,593
AstraZeneca:						
U.S. / RoW Agreement		439,000		810,000		1,249,000
China Agreement		77,200		299,500		376,700
Total AstraZeneca		516,200		1,109,500		1,625,700
Total revenue	\$	1,161,293	\$	1,382,000	\$	2,543,293

These collaboration agreements also provide for reimbursement of certain fully burdened research and development costs as well as direct out of pocket expenses.

RESULTS OF OPERATIONS

Revenue

	Years Ended December 31,							Change 2020 vs	. 2019
	2020		2019		2018			\$	%
				(0	dollars	in thousand	s)		
Revenue:									
License revenue	\$	14,323	\$	177,086	\$	22,269	\$	(162,763)	(92) %
Development and other revenue		80,592		114,115		125,913		(33,523)	(29) %
Product revenue, net		72,498		1,700		-		70,798	4,165 %
Drug product revenue		8,906		(36,324)		64,776		45,230	(125) %
Total revenue	\$	176,319	\$	256,577	\$	212,958	\$	(80,258)	(31) %

Our revenue to date has been generated substantially from our collaboration agreements with Astellas and AstraZeneca. In addition, we started roxadustat commercial sales in China in the third quarter of 2019.

Under our revenue recognition policy, license revenue includes amounts from upfront, non-refundable license payments and amounts allocated pursuant to the standalone selling price method from other consideration received during the periods. This revenue is generally recognized as deliverables are met and services are performed. License revenues represented 8%, 69% and 11% of total revenues for the years ended December 31, 2020, 2019 and 2018, respectively.

Development revenue includes co-development and other development related services. Co-development services are recognized as revenue in the period in which they are billed to our partners, excluding China. For China co-development services, revenue is deferred until we begin to transfer control of the manufactured commercial drug product to AstraZeneca.. Other development related services are recognized as revenue over the noncontingent development period based on a proportional performance method. As of December 31, 2020, the estimated future non-contingent development periods range from 3 to 48 months. Other revenues consist of sales of research and development material and have not been material for any of the periods presented. Development and other revenues represented 46%, 44% and 59% of total revenues for the years ended December 31, 2020, 2019 and 2018, respectively.

We started generating net product revenue from commercial sales of roxadustat drug product in China in the third quarter of 2019. Product revenue is recognized when our customer obtains control of promised goods or services in an amount that reflects the consideration we expect to receive in exchange for those goods or services. Product revenue represented 41% and 1% of total revenue for the year ended December 31, 2020 and 2019, respectively.

Drug product revenue includes commercial-grade API or bulk drug product sales to AstraZeneca and Astellas in support of pre-commercial preparation prior to the NDA or MAA approval, and to Astellas for ongoing commercial launch in Japan. Drug product revenue is recognized when we fulfill the delivery obligations. The amount of variable consideration that is included in the transaction price may be constrained, and is included in the drug product revenue only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period when the uncertainty associated with the variable consideration is subsequently resolved. Actual amounts of consideration ultimately received in the future may differ from our estimates, for which we will adjust these estimates and affect the drug product revenue in the period such variances become known. Drug product revenues represented 5%, (14)% and 30% of total revenues for the years ended December 31, 2020, 2019 and 2018, respectively.

In the future, we will continue generating revenue from collaboration agreements in the form of license fees, milestone payments, reimbursements for collaboration services and royalties on product sales, and from product sales. We expect that any revenues we generate will fluctuate from quarter to quarter due to the uncertain timing and amount of such payments and sales.

Total revenue decreased \$80.3 million, or 31% for the year ended December 31, 2020 compared to the year ended December 31, 2019 for the reasons discussed in the sections below.

License Revenue

	Years Ended December 31,						Change 2020 vs. 2019		
	 2020		2019		2018		\$	%	
			(0	lollars	in thousands)			
License revenue:									
Astellas	\$ 14,323	\$	129,405	\$	14,323	\$	(115,082)	(89) %	
AstraZeneca	-		47,681		7,946		(47,681)	(100)%	
Total license revenue	\$ 14,323	\$	177,086	\$	22,269	\$	(162,763)	(92) %	

License revenue decreased \$162.8 million, or 92% for the year ended December 31, 2020 compared to the year ended December 31, 2019.

License revenue recognized under our collaboration agreements with Astellas decreased \$115.1 million, or 89% for the year ended December 31, 2020 compared to the year ended December 31, 2019. License revenue recognized under our collaboration agreements with Astellas for the year ended December 31, 2020 represented the allocated revenue of related to a regulatory milestone of \$15.0 million associated with the NDA approval in Japan achieved during the fourth quarter of 2020. License revenue recognized under our collaboration agreements with Astellas for the year ended December 31, 2019 represented the allocated revenue of \$117.5 million related to two regulatory milestones totaling \$130.0 million associated with the planned MAA submission in Europe that were included in the transaction price during the second quarter of 2019 when these milestones became probable of being achieved; and the allocated revenue of \$11.9 million related to a regulatory milestone of \$12.5 million associated with the NDA approval in Japan achieved during the third quarter of 2019.

We did not have any license revenue under our collaboration agreements with AstraZeneca for the year ended December 31, 2020. License revenue recognized under our collaboration agreements with AstraZeneca for the year ended December 31, 2019 represented the revenue allocated to the U.S./RoW license of \$33.1 million related to a regulatory milestone of \$50.0 million associated with the NDA submission in the U.S. that was included in the transaction price during the second quarter of 2019 when this milestone became probable of being achieved; and the revenue allocated to the U.S./RoW license of \$14.6 million related to three regulatory milestones totaling \$22.0 million associated with roxadustat being included on the updated NRDL released by China's NHSA during the fourth quarter of 2019.

Development and Other Revenue

	Years Ended December 31,							Change 2020 vs. 2019		
	2020		2019		2018		\$		%	
			(dollars in thousands							
Development revenue:										
Astellas	\$	19,174	\$	29,394	\$	20,903	\$	(10,220)	(35) %	
AstraZeneca		61,418		84,719		104,970		(23,301)	(28) %	
Total development revenue		80,592		114,113		125,873		(33,521)	(29) %	
Other revenue		-		2		40		(2)	(100)%	
Total development and other revenue	\$	80,592	\$	114,115	\$	125,913	\$	(33,523)	(29) %	

Development and other revenue decreased \$33.5 million, or 29% for the year ended December 31, 2020 compared to the year ended December 31, 2019

Development revenue recognized under our collaboration agreements with Astellas decreased \$10.2 million, or 35% for the year ended December 31, 2020 compared to the year ended December 31, 2019. Development revenue recognized under our collaboration agreements with Astellas for the year ended December 31, 2020 included the allocated revenue of \$0.7 million related to the above-mentioned \$15.0 million associated with the NDA approval in Japan achieved during the fourth quarter of 2020. Development revenue recognized under our collaboration agreements with Astellas for the year ended December 31, 2019 included the allocated revenue of \$11.4 million related to the above-mentioned \$130.0 million associated with the regulatory milestones of the planned MAA submission in Europe, and the allocated revenue of \$0.5 million related to the above-mentioned \$12.5 million associated with the NDA approval in Japan. The decrease for the year ended December 31, 2020 was partially offset by an increase in co-development billings related to related to higher medical affairs activities under the Europe Agreement.

Development revenue recognized under our collaboration agreements with AstraZeneca decreased \$23.3 million, or 28% for the year ended December 31, 2020 compared to the year ended December 31, 2019, primarily due to a decrease in co-development billings related to the development of roxadustat as a result of the substantial completion of Phase 3 trials for roxadustat. Development revenue recognized under our collaboration agreements with AstraZeneca for the year ended December 31, 2019 also included the allocated revenue of \$9.3 million related to the above-mentioned \$50.0 million associated with the regulatory milestone of the NDA submission in the U.S., and the allocated revenue of \$4.1 million related to the above-mentioned regulatory milestones totaling \$22.0 million associated with roxadustat being included on the updated NRDL released by China's NHSA.

Product Revenue, Net

		Years Ended	Decen	ıber 31,	Change 2020 vs. 2019			
	2020			2019	\$	%		
				ısands)				
Gross revenue	\$	89,027	\$	2,803 \$	86,224	3,076 %		
Price adjustment		-		(936)	936	(100) %		
Non-key account hospital listing award		(9,325)		-	(9,325)	100 %		
Contractual sales rebate		(6,189)		(149)	(6,040)	4,054 %		
Other discounts and rebates		(923)		(18)	(905)	5,028 %		
Sales return		(92)		-	(92)	100 %		
Product revenue, net	\$	72,498	\$	1,700	70,798	4,165 %		

We started roxadustat commercial sales in China in the third quarter of 2019. Therefore, the year-over-year comparison would not be meaningful, as the prior year was at limited sales volume.

The gross product revenue for the year ended December 31, 2020 was \$89.0 million.

In the second quarter of 2020, we amended the agreement with our pharmaceutical distributors, which triggered accounting modifications particularly related to non-key account hospital listing award. For the year ended December 31, 2020, the non-key account hospital listing award was \$9.3 million, which was recorded as a reduction to the revenue and calculated based on eligible non-key account hospital listing to date achieved by each distributor with certain requirements met during the period.

Exhibit 31.1

CERTIFICATION

- I, Enrique Conterno, certify that;
- 1. I have reviewed this annual report on Form 10-K of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in the Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2021

/s/ Enrique Conterno
Enrique Conterno
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

- I, Pat Cotroneo, certify that;
- 1. I have reviewed this annual report on Form 10-K of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in the Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2021

/s/ Pat Cotroneo

Pat Cotroneo
Senior Vice President, Finance and Chief Financial
Officer (Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Enrique Conterno, Chief Executive Officer of FibroGen, Inc. (the "Company"), and Pat Cotroneo, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

- 1. The Company's Annual Report on Form 10-K for the year ended December 31, 2020 (the "Annual Report"), to which this Certification is attached as Exhibit 32.1, fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and
- 2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

In Witness Whereof, the undersigned have set their hands hereto as of the 1st day of March, 2021.

/s/ Enrique Conterno
Enrique Conterno
Chief Executive Officer

/s/ Pat Cotroneo
Pat Cotroneo
Senior Vice President, Finance and Chief Financial Officer

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of FibroGen, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.

EXHIBIT 00

S&P Global
Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Tuesday, March 02, 2021 5:50 PM GMT

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Call Participants

EXECUTIVES

Enrique A. Conterno CEO & Director

ANALYSTS

Brendan Mychal Smith *Cowen and Company, LLC, Research Division*

Yaron Benjamin Werber Cowen and Company, LLC, Research Division

Presentation

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And good afternoon, everybody, and thank you for joining us for the second day of the 41st Annual Cowen Healthcare Conference. I'm Yaron Werber, biotech analyst here at Cowen with my colleague, Brendan Smith. And it's a great pleasure for us to moderate the fireside chat with FibroGen.

Today, we have Enrique Conterno, who's the CEO; and Mike Tung, VP of Investor Relations and Strategy. Gentlemen, thanks so much for joining us. We appreciate it.

Enrique A. Conterno

CEO & Director

Thank you very much for the invitation, Yaron.

Question and Answer

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Absolutely. So Enrique, maybe the timing for this is good in a way, just given some of the news from yesterday, obviously, wasn't herbed our ways by chance. But maybe give us a little bit of a sense related to the news flow from yesterday, what you can share with us on the interaction with FDA or the next steps in the process?

Enrique A. Conterno

CEO & Director

Yes. Maybe -- I do appreciate the opportunity to be able to share. We had our earnings call yesterday. So this is an opportunity to basically maybe describe some of the events. And let me start with the extension that we had. As you know, last December, in the final stages of review, the FDA extended the review period of the roxadustat NDA by 3 months to review additional analysis of clinical data.

And at that time, set a new PDUFA date of March 20, 2021. Yesterday, we were informed by the FDA that they plan to hold an advisory committee or an Adcom to review the NDA for roxadustat in the U.S. We have not received a confirmed date for this planned outcome. We were surprised by the request, I think in 3 separate occasions. The FDA let us know that they were not planning to hold an Adcom at that time, whether it was -- when the NDA filing was accepted during the mid-cycle review and then in the late cycle review.

It is not unusual for the FDA to hold an Adcom for a first-in-class new molecular entity. And in fact, we shared last spring that we were preparing for -- very much for that possibility. So now I think for us, we are refocusing our efforts on resuming those activities. I'm very much looking forward now to presenting the comprehensive roxadustat data in that public saying. We continue to have confidence in the completeness of the NDA submission and the strength of the roxadustat data. And we're very much -- both FibroGen and AstraZeneca committed to working with the FDA to bring roxadustat to patients with an anemia CKD in the U.S. as soon as possible.

So clearly, as you can appreciate and as we've mentioned this in the past, we are not in a position to discuss the detail of our FDA interactions, but I look forward to having discussion about this topic. And of course, I think also the broader agenda that FibroGen has.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Absolutely. So Enrique, just to set the stage a little bit, historically. My impression is that ESAs were originally submitted for approval 25 years ago to the Hematology division, and I believe ODAC probably reviewed them back then. About 13, 14 years ago, during the FDA's review of the safety issues of ESAs, remember, there was a -- I think it was 2007, there was a cardiorenal committee that look at dialysis and pre-dialysis in 2008, it was about a year later, ODAC reviewed relating to the safety issues of oncology.

Roxa was filed to the Hematology division. Can you give us the history on that? And how did cardiorenal this time around get involved, the Cardiorenal division within the review?

Enrique A. Conterno

CEO & Director

Yes. I think it's a really good question. So let's take it step by step. First, I think, clearly, roxa was filed with the Hematology division. Keep in mind that the Hematology division that we're speaking of is part of the office of the ocean office. So this includes cardiology, hematology, endocrinology and nephrology which are all part of that division.

There was a realignment where benign hematology basically was brought into in that office separately from the rest of oncology. So it is part of the same office, and it is that office and cardiorenal is -- it is part of that same office, right? In the past, when you're thinking about ODAC, the alignment of the FDA of the divisions to the office was different. Hematology was basically part of a different office.

So that realignment occurred, if I remember correctly, maybe about 18 months ago. So it is not -- we don't view it as unusual for cardiorenal to be focused on the host in the advisory committee. And quite frankly, we view it as a positive for us. We think that we will have the appropriate expertise to make sure that the product is reviewed with -- through -- with nephrologists and cardiologists' inputs.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And so do you have a sense on how did cardiorenal get involved? Was there a request from hematology? Do they need to ask cardiorenal for help, and that's ultimately how an Adcom is called for by cardiorenal, just logistically, how does things even work between divisions?

Enrique A. Conterno

CEO & Director

Honestly, I don't know that question. But I do know that it is the office really, that is -- has discretion to call for the Adcom. And at this point in time, it's a cardiorenal Adcom. And we just look forward to presenting the data. But I don't know the -- how that decision was made by the FDA.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And have all the interactions so far, during the review process, been with hematology? Or was there some interaction with cardiorenal at some point, given this is a renal indication?

Enrique A. Conterno

CEO & Director

Yes. No, really, I think that review has been with the hematology division, we do not know, of course, the interaction within the agents itself.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Got it. And has there been any change in the reviewers at FDA side?

Enrique A. Conterno

CEO & Director

We're not commenting, as you know, on our FDA interactions or any type of details. I think at this point in time, I think our -- and keep in mind that these news are also -- we were informed yesterday, literally. So at this point in time, our focus is on basically preparing. As you can imagine, we need to look for any type of precedent here is what are some of the precedence we will do some work around that.

But at the end, I think we know that an Adcom is an opportunity to basically showcase, I think, the strength of our data, and we continue to have confidence on the strength of the data of roxadustat across both DD and NDD.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And for a long time from your interaction with FDA, I think the comments to you were that FDA was not planning on calling an Adcom at that time. And that can always obviously change over time. Any sense -- it sounds like you're literally sort of on the 1-yard line, it was sort of the sense we're getting both from your comment and AstraZeneca's comments, when there was a last-minute request for more information, probably somewhere high up in the division. I imagine, at that point, it's probably the last review, sort of a

higher up in the division. So any -- can you give us just chronologically maybe what happened that led to the, obviously, the PDUFA extension and now to the Adcom?

Enrique A. Conterno

CEO & Director

Yes. I think as you mentioned, we were in the -- very much in the final stages of our review. I think we had mentioned that we were in label negotiation back -- all the way back since maybe August, late August, early September. And we -- very late in the review, we were requested additional analysis, which basically, given the imminence of the PDUFA date, basically required a PDUFA extension.

It is -- we've gone through those. We, of course, submitted the requested analysis. And at this stage, I think we were notified by the FDA that they are requesting an Adcom. It's difficult for us, as you can imagine, to speculate on the rationale for calling an Adcom. An Adcom is -- was very much a possibility throughout the review, but it's highly unusual at this stage in the process, right? So had you asked me a year ago, I would have said that was very much a possibility.

In fact, we were very upfront that we were preparing for one. But -- and quite frankly, it is an opportunity for us to basically discuss the data in a public forum. The issue is really the timing, right, than the overall process.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

I guess it's more of an issue. I mean, obviously, that could delay approval time lines, but is the issue more along the lines that now that PDUFA will lapse the March 20 PDUFA, by definition, is going to have to lapse just given the statue to give you almost 2 months' notice before a panel is called. The -- so is the next step for the FDA to give you a -- announce an Adcom and you go to an Adcom and thereafter, they'll finish their review or they're not going to finish the review, give you correspondence -- official correspondence and then have a panel, right?

Enrique A. Conterno

CEO & Director

No, I think a panelist can be held under an ongoing review. So I think, yes, I think the PDUFA date under this scenario would lapse, and the PDUFA date is March 20 of this year, so it's coming up quickly. And the FDA will probably notify us of the dates for the Adcom. And then I think post the Adcom being held, I think the FDA will basically make a decision. But there would not be a new PDUFA date given the PDUFA date can only be extended once.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

One of the questions -- I'm sort of taking questions as they come along. On the question is, to the extent, in the best of your ability what you can comment on, what do you think might be discussed at an Adcom? What could be some of the topics that FDA and also you would want to air publicly during an Adcom?

Enrique A. Conterno

CEO & Director

I think during the Adcom, I think typically, broadly, you want to basically showcase the benefit risk profile of the product across both of DD indications, DD and NDD. And -- but it's difficult for us at this stage without receiving the formal notification and having a discussion -- a fuller discussion with the FDA for us to speculate right now on the focus of the Adcom.

I think we will learn more of that as time goes by, and we engage with the FDA. And even at that point in time, I think we will have to make -- we will need to have a view of what is that we will be able to share at that point.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Has there been any more data requests since submitted the data, I presume around December 20?

Enrique A. Conterno

CEO & Director

Yes. We're not commenting on that. What I can say is that all analysis that were requested were submitted.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Okay. Okay. Understood. I mean is this a case where hematology just doesn't feel that they have the right expertise in the renal space to be able to review, and that's the reason that the they're calling an Adcom? Or is it by definition? If they were to call a hematology Adcom, it would be composed of hematologists, which is probably not best suited for this product. So by definition, they have to go through cardiorenal to convene an Adcom?

Enrique A. Conterno

CEO & Director

I think if you look at it logically and given the expertise in nephrology and importance -- the importance to get the clinical feedback from nephrologists, I do think that cardiorenal is not only a logical choice, but also the welcome choice, I think, in our view, in terms of holding this Adcom. So we view that not just a profit, but the opportunity to ensure that we have -- and the expert review basically with the comments from all the appropriate expert parties.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Yes. I recall from some of your previous comments and also from your partners, AstraZeneca, based on the totality of the data for roxa, you're fairly comfortable, optimistic that the data should support a broad label. And the impression we were all getting is that you're marching towards that sort of outcome. When we look at the totality of the data, there is much less questions, at least in our view, in dialysis, given the alignment with the regulatory agencies ahead of time, entity was admittedly, be at risk. The protocol wasn't agreed to, and it was a reasonable protocol, but there was ultimately a lot of crossover.

There was -- the study was complicated. And the physical analysis was complicated. So when I think of the 2, we think dialysis is probably a huge unmet need. Non-dialysis, no product approved, maybe not quite as urgent and probably more complicated review process. Does that make sense, in your view, maybe is that something that might be discussed along the line?

Enrique A. Conterno

CEO & Director

Honestly, I think we feel highly confident about both DD and NDD. We think that the data, I think, supports -- the benefit risk profile, I think, supports both indications, the use of roxadustat, I think, across both populations. I know because we've discussed in the past, and I think I've been pretty clear in terms of what has been agreed with the FDA and what hasn't been agreed with FDA. I think that's known.

And at this point in time, we're heading through to an Adcom, I think, so we'll have the opportunity to fully showcase. Keep in mind, I think, also, I think when it comes to NDD, yes, we conducted our studies against placebo, but we did have a pretty significant impact on the reduction of transfusions. And when you look at the hazard ratio, it was 0.26. So really, really significant benefits in terms of lowering risk of transfusions.

We've also presented data from our clinical trials, the risk of transfusions dramatically increases for hemoglobin below 10 versus above 10, almost -- there's a 3 to 5x increase. So the opportunity for a product, for roxadustat, I think is very significant. Keep in mind that most of the NDD population is not

treated. We've shared that maybe about 14%, 15% of the population that goes to dialysis receive ESAs in the 12 months prior to going on to dialysis, that's really -- for people that are very late-stage with chronic kidney disease, that's pretty low number. So I think the opportunity here is basically to be able to treat many more patients, so that patients can benefit. And then we think the roxa can play a very important role there.

Yaron, I think you're on mute right now.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Yes. Thank you for that. The studies, I think yesterday, you mentioned on the call that the ASPEN and DENALI studies in the large -- well, we think in large dialysis clinics have completed enrollment in the dialysis setting. When -- is that data that you will share externally? Or is that data that was designed more to help those clinics understand about how to switch and how to incorporate roxa into their protocols?

Enrique A. Conterno

CEO & Director

I think both. We will -- we intend to share the data at an appropriate conference. But clearly, I think it is also allowing for us to understand roxadustat. I think the very specific settings are not -- yes, these are clinical trials, but in the very specific settings of dialysis or large dialysis organizations and thinking about the particular product also. It is important trials, and we are pleased that, that enrollment has concluded. And now I think we expect to report data in the second half of this year.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And so those are going to be essentially open-label studies that are going to looking at outcomes, pharmaco...

Enrique A. Conterno

CEO & Director

Yes. Yes, it's going to be looking at a number of factors. Clearly, the efficacy and safety of roxadustat was established by the global Phase III program, the pivotal Phase III programs, are known 3 programs in DD and 3 programs in NDD in terms of the submission to the FDA. And I think in this particular case, is just very specific trials adapted to the needs of the dialysis organizations to look at outcomes that they will be very much interested.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Okay. The -- when you think about one of the novelties of roxa is that there was an incident dialysis population, the prevalent dialysis population. And you haven't reported the data in incident dialysis. I mean obviously, presumably, you would expect -- you would ask for a broad label. I'm just trying to think about all the nuances during a review, discussion, the flexibility of dosing and dosing parameters, just parameters relating to switching from an ESA to roxa.

And then there's a complexity of other companies in the space mentioned that they were in agreement with FDA to run an NDD study against an ESA, and there was an understanding within that context, those modulators will inherit an ESA-like black box. When I think of a drug like roxa, you have your own parameters around your studies. ESAs have their own black box and many -- in many ways because of cancer promotion data, which is not relevant to roxa. So as I think about all the topics think you think are going to be critical for you and FDA to align on to then write a label, what are the parameters are we missing that maybe I didn't kind of bring up?

Enrique A. Conterno

CEO & Director

Yes. You're asking me to speculate on the thinking of the FDA here. But I think in general, I think the rationale that we provided for and the discussion that we had with the FDA at that time. And the rationale for conducting the trials related to placebo was related to most patients are untreated in this population. By the way, placebo is a higher hurdle, right? And when you look at the overall results, we showed comparability when it comes to these outcomes in the population.

So we feel good about our results. Now at the end, I think we need to go through the outcome, I'll be able to have a discussion for us to be able to fully answer, I think, the questions that you're asking.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Just remind us in pre-dialysis and maybe for both, the agreed-upon upper bound of the confidence interval, just remind us what you said publicly.

Enrique A. Conterno

CEO & Director

Yes. We -- what I said public is that there was no agreed-upon upper bound. I always commented, this was always a review issue with the FDA, meaning, at the end, the FDA needs to look at all of this data, and there's no established guidance, I think, in this particular therapeutic area. There is established guidance in diabetes when there is a particular upper bound of 1.8 to approve of product on 1.3 long-term to be able to -- for the probe to show and be able to exclude that risk of more than 30% potential increase.

I think in our case, and that's not something that -- what we agree with the FDA, the agreement that we had was related to the trial that will be included in the analysis and the submission as well as the statistical methodology that would be used. Clearly, throughout the review and as part of our submission, we always do a number of sensitivity analysis with the FDA, and we included that as part of our package. But 1.3 was not agreed upon pre-defined agreement on upper bound with the FDA.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And you're talking about both dialysis and pre-dialysis? Or you're mentioning in pre-dialysis?

Enrique A. Conterno

CEO & Director

I'm speaking broadly, broadly. Yes.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Okay. Yes. And I think the discussion really has been even with some of your competitors more in the 1 point -- the 15% and the 25% sort of range between FDA and EMA?

Enrique A. Conterno

CEO & Director

Yes. Clearly, I think when you look at -- I cannot speak for the comments of our competitor, but in your question about NDD, I think it's pretty clearly -- we basically would meet that anyways. But -- and even though we were relative to placebo, which is a higher hurdle from a safety perspective. I -- you also spoke about the dialysis population and you may recall that we presented, in particular, we're very excited and continue to be very excited about the incident dialysis data, where we basically show the statistical significant reduction on both MACE and MACE+ outcomes in that population.

And so we also think that, that's quite significant and quite important, given that, that's when the decision for a new anime treatment is made for patients that are started dialysis.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And what about with EMA? I think with EMA, if I -- my recollection is that there was more agreement and alignment. Can you maybe just discuss what you said publicly about that?

Enrique A. Conterno

CEO & Director

We haven't commented on EMA, I think Astellas is the sponsor for EMA not FibroGen. And FibroGen, we were the ones that submitted the NDA. That review is ongoing, and I think what we shared yesterday was that we expect the decision sometime around the middle of the year.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

And that's from the CHMP initially?

Enrique A. Conterno

CEO & Director

Well, just yes, not just an opinion, but we are -- my comments about the beginning of the year is around approval.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Around approval? Okay, right. So we should even find out over the next maybe even 1 or 2 months really, but depending on the definition of -- from the CHMP. Okay. I -- Brendan, do you want to ask maybe [Audio Gap] and MDS?

Brendan Mychal Smith

Cowen and Company, LLC, Research Division

Sure. Sure. Yes, I know you have a couple of other studies going on outside of the CKD anemia space. So can you kind of just give us a really quick update with the enrollment status is for the MDS study and CIA. And kind of just confirm when we're going to see data from each of these and what that would maybe look like?

Enrique A. Conterno

CEO & Director

Yes. I think CIA is fully enrolled, and we expect to have basically the readout for that in the second half of this year, that's a Phase II study. And assume this study is positive, we expect to start of the phase III trial in chemo-induced anemia. The opportunity is very significant, and we basically, from a scale perspective, magnitude perspective, the opportunity is almost comparable to the opportunity that we see across CKD anemia. In the case of MDS, this is a Phase III trial, which is ongoing. And we've shared that we expect to report data in the first half of next year.

And clearly, I think it's very much an unmet medical need. And we feel that roxadustat can be an important treatment option in that setting. Of course, we need to wait for the Phase III results, but we are looking forward to concluding the trial as soon as possible.

Brendan Mychal Smith

Cowen and Company, LLC, Research Division

Got it. So I mean, obviously, MDS is kind of exploded with competition more recently. So I guess, can you kind of give us just a sense of how you're approaching the commercial opportunity there? And where you really see roxa kind of fitting in versus some of the other options that are available?

Enrique A. Conterno

CEO & Director

Yes. I think there's been additional options that are available today. I think those options tend to have a narrower set of patients or indications, although they are pursuing studies that are broader. Keep in mind, in our studies, we include both R positive and R negative patients, and also patients that were regardless of failure to ESAs agents. So we feel that the roxadustat's approach basically covers a very significant amount of patients. So we could have broad applicability, of course, we need to look at the results. But the results so far that we've seen, I think, tend to indicate that we have a product that is effective, and we need to see the final Phase III results to fully understand the profile of the product.

But we feel confident about our -- the potential utilization of roxadustat in this scene.

Brendan Mychal Smith

Cowen and Company, LLC, Research Division

Okay. Great. And I know we just have a couple of minutes left. I want to ask 1 quick one on pamrevlumab. Obviously, you have studies in IPF, in pancreatic cancer, now DMD, or plan to start the non-ambulatory DMD pretty soon. So can you -- I guess, just maybe on IPF here because I think this is the one that gets a lot of attention for the drug itself. You're going to have these 2 different studies. Obviously, COVID is an issue here for these patients. But can you kind of give us an idea of what you're really hoping to see from that Phase III that would really kind of reinforce confidence that it's maybe a particular endpoint that you think is really most important and kind of what extensive improvement and maybe kind of your plans for the readout in trials?

Enrique A. Conterno

CEO & Director

Yes. So clearly, what we -- the best example, what we expected, we want to replicate the studies -- basically the results that we saw in Phase II. They showed a very significant affect size. When it comes to the FDA, I think the primary endpoint is forced viral capacity. So -- and the Phase II results looked at that and a very significant impact in that. Keep in mind that in the case of pamrevlumab, not only do we have great results when it comes to forced vital capacity, but also we were able to show through imaging, basically really improvements when it comes to fibrosis. So not only is the biology, really promising here, but clearly, we have clinical data in Phase II that is quite impressive. And we made literally very few changes in the Phase III program. So we feel that the program is -- the likelihood of technical success, we believe, is very high.

We are trying to make sure that we execute as well as we can. COVID has been a pretty significant challenge when it comes to enrollment in these trials, just given the vulnerability of these patients. As we see now with the failure of the Galapagos trial, that has opened up a number of additional sites for us to be able to recruit sites in the past we did not have full access to. So we've already started that process contacting, and we've already added a number of sites. But also patients that were enrolled in those trials that might be eligible or could be eligible to enroll in the IPF, the ZEPHYRUS trials for pamrevlumab.

So that's probably an opportunity for us to accelerate the enrollment. We've also commented on our expansion of sites throughout the world, but also geographically, including China. So we've basically kind of pulled a number of levers to basically improve enrollment, and we're seeing some of that.

Brendan Mychal Smith

Cowen and Company, LLC, Research Division

Okay. Great. I think we're right up against time. And last questions from you, Yaron?

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

No. I think that warps it up. So Enrique and Mike, thanks so much for joining us. We really appreciate it.

Enrique A. Conterno

CEO & Director

Thank you very much, Yaron and Brendan.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division

Absolutely. Stay safe, and we'll be in touch.

Enrique A. Conterno

CEO & Director

Bye-bye.

Yaron Benjamin Werber

Cowen and Company, LLC, Research Division Thank you.

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EXHIBIT PP



Source: FibroGen, Inc.

April 06, 2021 16:01 ET

FibroGen Provides Additional Information on Roxadustat

Company Continues to be Confident in the Benefit / Risk Profile of Roxadustat

Company to Host Investor Call Today at 5:00 p.m. Eastern Time (2:00 p.m. Pacific Time)

SAN FRANCISCO, April 06, 2021 (GLOBE NEWSWIRE) -- FibroGen, Inc. (Nasdaq: FGEN) (the "Company") today provided clarification of certain prior disclosures of U.S. primary cardiovascular safety analyses from the roxadustat Phase 3 program for the treatment of anemia of chronic kidney disease ("CKD").

"As members of senior management were preparing for the upcoming FDA Advisory Committee meeting, we became aware that the primary cardiovascular safety analyses included post-hoc changes to the stratification factors," said Enrique Conterno, Chief Executive Officer, FibroGen. "While all of the analyses set forth below, including the differences in the stratification factors, were included in the NDA, we promptly decided to clarify this issue with the FDA and communicate with the scientific and investment communities."

Mr. Conterno continued, "It is important to emphasize that this does not impact our conclusion regarding the comparability, with respect to cardiovascular safety, of roxadustat to epoetin-alfa in dialysis-dependent (DD) patients and to placebo in non-dialysis dependent (NDD) patients. We continue to have confidence in roxadustat's benefit risk profile."

FibroGen continues to prepare for the FDA Advisory Committee meeting and will work closely with the FDA to bring this important new treatment to patients living with anemia of CKD.

There is no change in the underlying roxadustat data, or to the efficacy analyses from the Phase 3 program. The Company has begun a comprehensive internal review to ensure such issues do not occur in the future.

Pooled Cardiovascular Safety Data

As previously disclosed, the Company agreed with the FDA in the pre-NDA meeting that the primary analysis in non-dialysis would be ITT (intention to treat with long-term follow up) and in dialysis would be OT-7 (on-treatment plus 7 days). MACE, a composite endpoint of all-cause mortality, stroke, and myocardial infarction, was the primary safety endpoint agreed on with the FDA.

The table below describes the cardiovascular safety results using the post-hoc stratification factors reported at the American Society of Nephrology conference in November 2019, as well as the analyses with the prespecified stratification factors which have not been previously publicly reported.

	Analyses with post-hoc stratification factors	Analyses with pre-specified stratification factors
	HR (95% Confidence Interval)	HR (95% Confidence Interval)
Non Dialysis (OLYM	IPUS, ANDES, ALPS N=4,270); ITT	
MACE	1.08 (0.94, 1.24)	1.10 (0.96, 1.27)
MACE+	1.04 (0.91, 1.18)	1.07 (0.94, 1.21)
ACM	1.06 (0.91, 1.23)	1.08 (0.93, 1.26)
Dialysis Dependent (HIMALAYAS, SIERRAS, ROCKIES N=3,880); OT-7		
MACE	0.96 (0.82, 1.13)	1.02 (0.88, 1.20)
MACE+	0.86 (0.74, 0.98)	0.91 (0.80, 1.05)
ACM	0.96 (0.79, 1.17)	1.02 (0.84, 1.23)
Incident Dialys	is (N=1,526); OT-7	
MACE	0.70 (0.51, 0.96)	0.82 (0.60, 1.11)
MACE+	0.66 (0.50, 0.89)	0.78 (0.59, 1.02)

ACM 0.76 (0.52, 1.11) 0.82 (0.57, 1.18)

ITT: intention to treat with long-term follow up

OT-7: on-treatment plus 7 days

Major Adverse Cardiovascular Event (MACE): a composite endpoint of all-cause mortality, stroke, and myocardial infarction.

(MACE+): in addition to the components in MACE, includes hospitalization due to heart failure or unstable angina.

(ACM): all-cause mortality.

As reflected in the table, the analyses with the pre-specified stratification factors result in higher hazard ratios (point estimates of relative risk) and 95% confidence intervals. For MACE+ in dialysis and for MACE and MACE+ in incident dialysis, the 95% confidence intervals include 1.0. While these hazard ratios remain below 1.0, based on these analyses we cannot conclude that roxadustat reduces the risk of (or is superior to) MACE+ in dialysis, and MACE and MACE+ in incident dialysis compared to epoetin-alfa.

These analyses do not change the Company's assessment that roxadustat is comparable to placebo in non-dialysis dependent patients and to epoetin-alfa in dialysis dependent patients using MACE to measure cardiovascular safety.

As previously announced, roxadustat has been launched in China and Japan for the treatment of anemia of CKD in both NDD and DD adult patients. These approvals were based on different studies conducted in the relevant geographies. In Europe, the Marketing Authorization Application for roxadustat for the treatment of anemia of CKD in patients both on dialysis and not on dialysis was filed by FibroGen's partner Astellas and accepted by the European Medicines Agency for review in May 2020.

Conference Call and Webcast Details

FibroGen will host a conference call and webcast today, April 6, 2021, at 5:00 pm Eastern Time (2:00 p.m. Pacific Time) to discuss this matter. Interested parties may access a live audio webcast of the conference call via the FibroGen website at https://fibrogen.gcs-web.com/events-and-presentations/events. It is recommended that listeners access the website 15 minutes prior to the start of the call to download and install any necessary audio software.

Dial-In Information

Live (U.S./Canada): (877) 658-9081 Live (International): (602) 563-8732 Confirmation number: 5297733

A replay of the webcast and investor presentation will be available shortly after the call for a period of 30 days. To access the replay, please dial (855) 859-2056 (domestic) or (404) 537-3406 (international), and use passcode 5297733.

About Anemia of CKD

Chronic kidney disease (CKD) is generally a progressive disease characterized by gradual loss of kidney function that may eventually lead to kidney failure or end stage renal disease, requiring dialysis or kidney transplant. CKD is estimated to occur in approximately 10-12% of adults worldwide and is predicted to become the fifth most common cause of premature death globally by 2040.

Anemia, a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, is a common early complication of CKD, affecting approximately 20% of CKD patients. Anemia of CKD is associated with an increased risk of hospitalization, cardiovascular complications, and death, and can also cause significant fatigue, cognitive dysfunction and reduced quality of life. Blood transfusions are used for treating severe anemia, however, they may reduce a patient's opportunity for kidney transplant and can increase the risk of infection and/or complications such as heart failure and allergic reactions.

About Roxadustat

Roxadustat, an oral medicine, is the first in a new class of medicines, HIF-PH inhibitors that promote erythropoiesis, or red blood cell production, through increased endogenous production of erythropoietin; improved iron absorption and mobilization; and downregulation of hepcidin. Roxadustat is also in clinical development for anemia associated with myelodysplastic syndromes (MDS) and for chemotherapy-induced anemia (CIA).

Roxadustat is approved in China, Japan, and Chile for the treatment of anemia of CKD in adult patients on dialysis (DD) and not on dialysis (NDD). In Europe, the Marketing Authorization Application for roxadustat for the

treatment of anemia of CKD in patients both on dialysis and not on dialysis was filed by our partner Astellas and accepted by the sarched by

Astellas and FibroGen are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia in territories including Japan, Europe, Turkey, Russia and the Commonwealth of Independent States, the Middle East, and South Africa. FibroGen and AstraZeneca are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia in the U.S., China, other markets in the Americas, in Australia/New Zealand, and Southeast Asia.

About FibroGen

FibroGen, Inc. is a biopharmaceutical company committed to discovering, developing, and commercializing a pipeline of first-in-class therapeutics. The Company applies its pioneering expertise in hypoxia-inducible factor (HIF) and connective tissue growth factor (CTGF) biology to advance innovative medicines for the treatment of unmet needs. The Company is currently developing and commercializing roxadustat, an oral small molecule inhibitor of HIF prolyl hydroxylase activity, for anemia associated with chronic kidney disease (CKD). Roxadustat is also in clinical development for anemia associated with myelodysplastic syndromes (MDS) and for chemotherapy-induced anemia (CIA). Pamrevlumab, an anti-CTGF human monoclonal antibody, is in clinical development for the treatment of locally advanced unresectable pancreatic cancer (LAPC), Duchenne muscular dystrophy (DMD), and idiopathic pulmonary fibrosis (IPF). For more information, please visit www.fibrogen.com.

Forward Looking Statements

This release contains forward-looking statements regarding the Company's prospects, including statements regarding the safety and efficacy profile of our product candidates and regulatory results, strategy and interactions, including those of our partners. Forward-looking statements include, but are not limited to, statements about our plans, objectives, representations and contentions and are not historical facts and typically are identified by use of terms such as "may," "will", "should," "on track," "could," "expect," "plan," "anticipate," "believe," "estimate," "predict," "potential," "continue" and similar words, although some forward-looking statements are expressed differently. Our actual results may differ materially from those indicated in these forward-looking statements due to risks and uncertainties related to the continued progress and timing of our various programs, including the enrollment and results from ongoing and potential future clinical trials, and other matters that are described in our Annual Report on Form 10-K for the fiscal year ended December 31, 2020 filed with the Securities and Exchange Commission (SEC), and the risk factors set forth therein, including without limitation, risks related to obtaining regulatory approval and the planned FDA Advisory Committee meeting. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and we undertake no obligation to update any forward-looking statement in this press release, except as required by law.

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EXHIBIT QQ

S&P GlobalMarket Intelligence

FibroGen, Inc. NasdaqGS:FGEN Special Call

Tuesday, April 06, 2021 10:00 PM GMT

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Presentation

Operator

Good day, and thank you for standing by. Welcome to the FibroGen Provides Roxadustat Update Call. [Operator Instructions] And please be advised that today's conference is being recorded. [Operator Instructions] I would now like to hand the conference to your speaker today, Michael Tung. Please go ahead.

Michael Tung

Investor Relations Executive

Thank you, Victor. Good afternoon, everyone. I'm Michael Tung, Vice President of Corporate Strategy and Investor Relations at FibroGen. Joining me on today's call are Enrique Conterno, our Chief Executive Officer; and Dr. Mark Eisner, our Chief Medical Officer. Format for today's call includes prepared remarks from Enrique and Mark. After which, we will open up the call for Q&A.

I would like to remind you that remarks made on today's call include forward-looking statements about FibroGen. Such statements may include, but are not limited to, statements regarding our collaboration with AstraZeneca and Astellas; results of clinical trials; our regulatory strategies and potential regulatory results; commercial results and results of operations; plans and strategy related to our business; and the planned FDA Advisory Committee Meeting and other anticipated FDA interactions. Each forward-looking statement is subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated in that statement. A more complete description of these and other material risks can be found in FibroGen's filings with the SEC, including our most recent Form 10-K.

FibroGen does not undertake any obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise. The press release reporting our business update and a webcast of today's conference call can be found on the Investors section of FibroGen's website at www.fibrogen.com. And with that, I'd like to turn the call over to Enrique Conterno, our CEO. Enrique?

Enrique A. Conterno

CEO & Director

Thank you, Mike. Good afternoon, and thank you all for joining us on such short notice. As you saw in today's press release, FibroGen is clarifying certain prior disclosures of U.S. primary cardiovascular safety analysis from the roxadustat Phase III program for the treatment of anemia of chronic kidney disease.

Let me explain more. The primary cardiovascular safety analysis included post-hoc changes to the stratification factors. The fact that this analysis included post-hoc changes to the stratification factors recently came to the attention of members of our senior management team, including myself, during our preparation for the upcoming FDA Advisory Committee meeting.

Before I continue, it is important to emphasize that there is no change in the underlying roxadustat data or to the efficacy analysis from the Phase III program.

Our conclusion regarding the comparability with respect to cardiovascular safety of roxadustat to epoetinalfa in dialysis-dependent patients and to placebo in nondialysis-dependent patients is not impacted. So let me be very clear. We continue to have confidence in roxadustat's benefit risk profile, and we're committed to working closely with the FDA to bring this important new treatment to patients living with anemia of CKD.

Nevertheless, we're taking this very seriously and promptly decided to clarify this issue with the FDA as well as communicate with the scientific and investment communities. We met with the FDA late last week. While all of the analysis set forth in the table provided today, including the differences in the stratification factors, were included in the NDA, we had a meeting with the FDA to ensure that it was clear. It was a

productive discussion, and we agreed to continue our discussion with regards to the advisory committee meeting. The team continues to prepare for this meeting.

Although this hasn't changed our confidence in roxadustat's benefit risk profile, and we believe this was limited to this particular set of analysis, we still want to understand how this happened. To that end, we have since begun a comprehensive internal review to ensure this doesn't occur in the future. This review is in its early stages. I don't have any additional details to share at this time.

I'll now turn it over to Mark Eisner, our Chief Medical Officer. Mark?

Mark Eisner

Chief Medical Officer

Thanks, Enrique. The press release the company issued today includes a table that describes the cardiovascular safety results using the post-hoc stratification factors reported at the American Society of Nephrology Conference in November 2019 as well as the analysis with the prespecified stratification factors which have not been previously publicly reported. This table is shown on the slide here, too.

As previously disclosed, the company agreed with the FDA in our pre-NDA meeting that the primary analysis in nondialysis would be ITT, or intention to treat, with long-term follow-up and in dialysis would be OT7, or on-treatment plus 7 days. MACE, a composite endpoint of all-cause mortality, stroke and myocardial infarction was the primary safety endpoint agreed on with the FDA. As you can see on this slide, the analysis with the prespecified stratification factors result in higher hazard ratios, point estimates of relative risk and 95% confidence intervals.

For MACE+ in dialysis and for MACE and MACE+ in incident dialysis, the 95% confidence intervals include 1. While these hazard ratios remain below 1, based on these analyses, we cannot conclude that roxadustat reduces the risk of or superior to MACE+ in dialysis and MACE and MACE+ in incident dialysis compared to epoetin-alfa. Importantly, these analyses do not change the company's assessment that roxadustat is comparable to placebo in nondialysis-dependent patients and to epoetin-alfa in dialysis-dependent patients using MACE to measure cardiovascular safety.

We have provided clarification, too, and we'll continue to work closely with the FDA, as Enrique mentioned at the start of today's call. I'd echo his comments that our recent discussion was a productive one, and our team remains focused on preparing for the upcoming Advisory Committee meeting.

Before I pass it back to Enrique, I'd also like to briefly touch on how this relates to our other launches for roxadustat. As previously announced, roxadustat has been launched in China and Japan for treatment of anemia of CKD in both NDD and DD adult patients. These approvals were based on different studies conducted in the relevant geographies. As such, we do not expect there to be an impact in China or Japan, where the product has already been launched.

And in Europe, the marketing authorization application for roxadustat for the treatment of anemia of CKD in patients both on dialysis and not on dialysis was filed by FibroGen's partner, Astellas, and accepted by the European Medicines Agency for review in May 2020. Based on our discussions with Astellas, we don't expect there to be an impact in Europe where the filing is currently under review.

With that, I'll turn it back over to Enrique for some closing remarks.

Enrique A. Conterno

CEO & Director

Thank you, Mark. I want to reinforce that we continue to have confidence in the roxadustat data and the safety and efficacy profile demonstrated in the Phase III program. In the U.S., we look forward to discussing the data in the upcoming Advisory Committee meeting and ultimately, to bringing this important new medicine to patients living with CKD anemia.

I hope it's clear that this team is focused on acting with full transparency and we're determined to ensure that something like this doesn't happen again. The senior management team is treating this with an utmost seriousness, as I emphasized at the start of today's call.

I'm not going to let this overshadow the incredible work that we have put into this treatment or the incredible work we are doing across the company to harness groundbreaking science to meet medical needs. Our 3 areas of focus, which you heard me talk about before, do not change as a result. First, we continue to be focused on ensuring the regulatory and commercial success of roxadustat, as we've emphasized throughout today's call. Second, we continue to be focused on accelerating the development of pamrevlumab in 3 high-value indications: locally advanced and resectable pancreatic cancer, Duchenne muscular dystrophy and idiopathic pulmonary fibrosis. And third, we continue to be focused on strengthening our research productivity based on leveraging our medical leadership position in both HIF and CTGF biology and accessing external innovation.

So what you're hearing from me is that while this internal review is ongoing, we'll continue to execute our business priorities to develop and deliver first-in-class medicines for the treatment of chronic and life-threatening conditions.

Now we will open the call for Q&A, keeping in mind that we will be limited in our ability to comment much beyond the detail we shared today.

Question and Answer

Operator

[Operator Instructions] Our first question will come from the line of Michael Yee from Jefferies.

[Technical Difficulty]

And our next question comes from the line of Geoffrey Porges with SVB Leerink.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

My questions relate to what was agreed on with the FDA. Enrique, first of all, did you present to the FDA previously in the original application, the post-hoc stratification based analysis or the prespecified stratification analysis? So to be clear, is this an issue of what was presented at ASN being inconsistent with what was provided to the agency? Or have you had to present new statistical -- your new statistical results to the agency?

And then secondly, it's fairly clear now that in the non-dialysis population, you have 2-point estimates that are above 1 in non-dialysis and the upper bounds of the hazard ratio -- of the confidence intervals above 1.25. Can you be clear whether the upper bound of the confidence intervals that was pre-agreed with the agency was 1.25 or 1.3 for noninferiority?

And then lastly, Do you still believe that you are non-inferior to placebo in the non-dialysis setting?

Enrique A. Conterno

CEO & Director

Yes. Very good. Thank you very much for your question, Geoff. I'll try to provide some initial answers, maybe to the last 2 parts of your question, and then I'm going to have Mark Eisner complement that.

Yes, we continue to believe that in non-dialysis, we basically show comparability relative to placebo. With regards to the 1 point to any measures of excess risk, you mentioned 1.25 or 1.3, I think I said in a number of different occasions that we do not have a pre-agreed non-inferiority margin with the FDA. That has always been a -- what we share as a review issue, an issue that needs to be looked at when the FDA looks at the totality of the efficacy and safety data for roxadustat.

When it comes to the NDA, we did submit a number of different analyses, including both sets of this analysis that we are sharing with you with the FDA. I'm going to Mark to maybe provide a little more context to that.

Mark Eisner

Chief Medical Officer

Yes. Thank you, Enrique. So yes, building on what you stated, we had previously included in the new drug application, both the analysis for the prespecified stratification factors and the post notification factors. And we also had explained the changes to the stratification factors in the new drug application. We met with FDA last week just to make sure that it was clear which analyses used which factors, prespecified and post-hoc, and the agency appreciated the clarification. It was a very cordial and collaborative meeting, and we agreed to continue working toward the Advisory Committee.

Operator

[Operator Instructions] Next question comes from the line of Difei Yang with Mizuho.

Difei Yang

Mizuho Securities USA LLC, Research Division

Just a couple. The first one is on have you been formally notified on the Adcom meeting, and if there is a schedule set up for that? And secondarily with regards to the internal review, is that an internal review of FibroGen's process? Or is that part of a NDA approval? So meaning that the FDA will have to buy into the conclusions and they think there's enough control this will not happen in the future.

Enrique A. Conterno

CEO & Director

Yes. Thank you, Difei. Let me answer the second part of your question. The internal review I was referencing is an internal FibroGen process. As it relates to the Adcom and the timing, we expect to hear from the FDA in the coming weeks on the timing of the Adcom.

As a reminder, we do not have an active PDUFA date at this time. And it would be, of course, consistent with prior practice for the FDA to make a decision on roxadustat NDA sometime after the Adcom. So we will be updating all of you once we learn more.

Operator

Your next guestion comes from the line of Michael Yee with Jefferies.

Michael Jonathan Yee

Jefferies LLC, Research Division

Hey guys, can you hear me okay now?

Enrique A. Conterno

CEO & Director

Yes.

Michael Jonathan Yee

Jefferies LLC, Research Division

Great. Yes. I'm not sure what happened, going on there. I have 2 questions related to dialysis. I just wanted to confirm that you are seeing that you cannot say you're superior in incident dialysis and get your view as to why you don't think that changes the overall benefit risk of the equation or perhaps even peak sales, maybe make a comment about that incident.

And then related to that, going again to your chart where you talk about dialysis. You showed total dialysis, you showed incident dialysis, but you don't show stable dialysis, which is the other half of the population. Can you maybe just comfort us or give some clarity as to what that data shows and why you don't think that's relevant.

Enrique A. Conterno

CEO & Director

Let us maybe try to answer all of those questions, maybe not the same order that you asked them. But clearly, our conclusions when it comes, as I mentioned, to -- in NDD and DD that we're comparable to placebo in NDD and comparable in DD to EPO have not changed a from a safety perspective. I think that's a critically important message.

When it comes to incident dialysis, the numbers continue to be quite positive. But at this stage, I think for MACE, it crosses 1. So we can no longer make the conclusion that we have a statistically superior result when it comes to MACE relative to EPO in this specific population.

Michael, this goes all the way to before my time. But FibroGen has been pretty clear over time that the fairest setting to be able to compare roxa relative to EPO is in the incident dialysis population. Those patients that are new to dialysis, in most cases, new to treatment, to look at how do they basically respond in each one of these treatments. And of course, over time, those incident dialysis patients become stable dialysis. So the incident dialysis patients here reflect -- yes, patients that were initiated within 4

months. But in -- those patients continued treatment, either on roxadustat or EPO, for some time through the conclusion of this trial.

When it comes to stable dialysis, that's something today, I think our focus has been, we have not published publicly data on stable dialysis today, I think our focus was really on providing an update on the data that we had publicly presented in the past. Clearly, this is something, when it comes to stable dialysis, we hear everyone that they want to see more data, and that's something we'll discuss with our partners. I'm going to ask Mark Eisner if he has something to add here.

Mark Eisner

Chief Medical Officer

Yes. Thanks, Enrique. I mean, the main thing I would add is that I would agree that the incident dialysis population is a very good population to look at the safety and efficacy of roxadustat because these patients are new to dialysis, they're just being started on the drug, and then they can transition onto dialysis with their anemia corrected. So that's point 1.

Point 2 is that the incident dialysis point estimates are still below 1. And the overall analysis are consistent with comparable safety to placebo in the NDD population and to ESA in the dialysis-dependent population. And overall, we feel very good about the overall benefit-risk profile of the drug.

Operator

Our next question comes from the line of Paul Choi with Goldman Sachs.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

I was wondering, first, if you could perhaps elaborate a little more on the stratification factors and which one, in terms of the change in between the post-hoc and the prespecified had the biggest impact with regard to the change to the point estimates and the confidence intervals? And then I have a follow-up.

Enrique A. Conterno

CEO & Director

Yes. I'm going to have Mark answer that question. We -- just to -- we have not conducted a specific analysis looking at each specific factor. So we looked at the combination of the factors, but I'll allow Mark to answer that question.

Mark Eisner

Chief Medical Officer

Yes. Thanks for the question. So the bottom line is that there were some post-hoc changes to the stratification factors. But to give you a little more detail, the cut point for GFR based on hemoglobin and definition of geographic region were changed after unblinding. And then in the dialysis-dependent population, there were some additional variables of sex, race and body mass index that were added. So this gives you kind of a sense for the types of changes that we're talking about.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Okay. And that clarification is helpful. My follow-up question is just with regard to the magnitude of the changes, specifically with regard to the incident dialysis population, which were -- which are larger than the changes to the NDD and DD population. And I guess here, just as you think about the comparability to the control arms here, I guess as you think about the incremental changes, especially to the upper ends of the confidence interval, I guess how -- what would your suggestion or what is the guidance here with regard to just thinking about the safety profile, given that the confidence intervals now are above 1 here.

Mark Eisner

Chief Medical Officer

So in the incident dialysis population, you're correct that the upper bounds for MACE and MACE+ now at 1. And for the dialysis-dependent population for MACE+, that's also true. But still, the overall results are very comparable in the NDD population to -- for roxadustat to placebo and in the DD and the incident dialysis subpopulation, comparable to ESA's in terms of cardiovascular safety. So overall, we continue to believe that the benefit risk profile of roxadustat is favorable.

Operator

And our next question comes from the line of Annabel Samimy with Stifel.

Annabel Eva Samimy

Stifel, Nicolaus & Company, Incorporated, Research Division

Most of them have been answered at this point. But I just want a little bit of clarification. First, when this issue came to your attention, was it something that you identified independently or was it brought to your attention by the FDA? Because I guess that changes maybe the tone of your conversations with the FDA.

And then the second question I had with regards to the NDD population. Ultimately, do you believe that this -- if you have to recommunicate this to the physician population, does this change their perception of the safety with regard to whether they might want to use it in NDD population. And ultimately, I guess, that goes back to the initial question, which was does this is change your peak potential here?

Enrique A. Conterno

CEO & Director

Yes. Thank you very much for your question. No, we were not informed of this by the FDA. I think the way this happen, as members of our senior management team were preparing for the upcoming FDA Adcom meeting, we became aware that the primary cardiovascular safety analysis including post-hoc changes to the stratification factors. And upon becoming aware, we promptly decided to clarify this issue with the FDA and communicate with the scientific and investment community. So that's how we should think about how this was uncovered. I'm going to allow now Mark to answer the second part of your question.

Mark Eisner

Chief Medical Officer

Thanks, Enrique. So you asked about specifically the non-dialysis dependent population and how we would communicate that to the physician community. And I think we can clearly state that the results with the prespecified stratification factors continue to support comparable cardiovascular safety between roxadustat and placebo and a positive benefit risk profile. So although we're now presenting you this information with the prespecified stratification factors, it's a very consistent message to the one that was communicated with the post-hoc stratification factors.

Operator

And our next question comes from the line of Jason Gerberry, Bank of America.

Unknown Analyst

This is [Claudia Herman] on for Jason. So to that point about the differences in MACE looking pretty minor, but in incident dialysis, it varies more presumably because of fewer events. Can you comment on the magnitude of the MACE components of stroke and MI, how those change in NDD? Is the lower end of the confidence interval still below 1?

Mark Eisner

Chief Medical Officer

So thanks for the question. As we've reiterated before, the primary analysis for cardiovascular safety is actually MACE in the nondialysis population and in the dialysis-dependent population, and we previously agreed that with FDA. And we also agreed in the NDD population with the intention to treat analysis in the OT7 approach for the dialysis-dependent analysis. So the primary safety is going to be based on the point

estimate and the 95% confidence interval for MACE. So that's the most important thing to emphasize here.

And we will be presenting the totality of the evidence at our Advisory Committee, including all of the other analysis that have been done to provide the most comprehensive picture of the benefit risk. And I think that's the most important thing to emphasize is the emphasis on MACE.

Unknown Analyst

Okay. And then when you say that the FDA agreed to ITT analysis for NDD and on-treatment analysis for DD, did they -- did the FDA themselves suggest this analysis? Or was it proposed by FibroGen? And do you think the FDA will also focus on the alternate analysis in each indication?

Mark Eisner

Chief Medical Officer

If I understand your question correctly, the question -- is the question about what stratification factors were agreed with FDA? I kind of missed it.

Unknown Analyst

It is on the ITT analysis for NDD and on-treatment analysis for DD. Did the FDA ask for that specifically? Or was it proposed by FibroGen? And do you think that the FDA will also look at on-treatment analysis for NDD and ITT analysis for DD?

Mark Eisner

Chief Medical Officer

I see your question. Apologies for not having it straight the first time. The FDA and FibroGen had a discussion at the pre-NDA meeting about the most appropriate analysis methodology. And both FibroGen and FDA agreed on the ITT analysis of MACE as primary for the non-dialysis population and the OT7 analysis for the dialysis-dependent population. So that was an agreement that was made, and it was thought to be, from both sides, the most appropriate way of presenting the data.

Now the other point I alluded to earlier about the totality of evidence, we clearly are going to present other analyses, for example, with the subset with EGFR greater than 10, ITT analysis with a landmark at 12 months, other sets of analyses that can be informative. And we think together, this will support the positive benefit-risk profile of roxadustat.

Operator

Your next guestion comes from the line of Yaron Werber with Cowen.

Brendan Mychal Smith

Cowen and Company, LLC, Research Division

This is Brendan on for Yaron. A lot of good ones here so far. So just a couple of quick ones here. Building on an earlier question about the stable dialysis patients, I just wanted to kind of check and narrow down. Do you have plans here or will you release data from the stable dialysis patients specifically to kind of offer this comparison versus full incident patients? And then I know you also mentioned that you don't really expect any impact to the China, Japan launches or the MAA filing. But have you had or maybe plan to have any conversations with EMA, for example?

Enrique A. Conterno

CEO & Director

Yes. The conversation in Europe really is led by Astellas. Astellas is the sponsor of the European submission. Our understanding, based on the discussion with Astellas, is that they don't expect this to impact the review. And I'm going to let Mark answer the first part of your question.

Mark Eisner

Chief Medical Officer

So the question again is about the stable dialysis data. And we, today, are really focusing on providing additional clarifications on scientific disclosures that have been already made, so we wanted to really focus on that. We do understand the SDD data are relevant for the investor and scientific community. And we are talking with our partners about the best way in which to present that information.

Enrique A. Conterno

CEO & Director

So the answer is yes, we intend to share that information in the future. Clearly, it is likely that, that information will be shared at the Adcom as well.

Operator

Your next question comes from the line of Andy Hsieh with William Blair.

Tsan-Yu Hsieh

William Blair & Company L.L.C., Research Division

So I have one kind of a follow-up to those question. So you mentioned that this discrepancy was discovered during the Adcom preparation. I'm just wondering is there any difference in the Adcom preparation last year versus this year that enabled the discovery of this discrepancy? And in your last week's discussion with the FDA, would you be able to share with us which division of the FDA you were speaking with? Was it the original NDA, the nonmalignant hematology division or the Adcom cardio-renal division?

Enrique A. Conterno

CEO & Director

Yes. I'm going to let Mark answer those 2 questions.

Mark Eisner

Chief Medical Officer

So in terms of your first part of your question, as Enrique said earlier, while we were reviewing the information, the NDA for preparing for the Adcom, it became clear that at the way the analysis have been done in terms of the pre versus post-hoc stratification factors has not been entirely clear. And recall that Enrique joined the company about 12 months ago, I joined about 4 months ago. So partly, this reflects fresh eyes on the same information. And we had a very good discussion with FDA, productive discussion about this, and they appreciated the clarifications.

In terms of the FDA discussion, specifically it was with Division of Hematology, which is conducting the review, and senior leadership from the Office of Cardiovascular, Hematology, Endocrinology and Nephrology (sic) [Office of Cardiology, Hematology, Endocrinology and Nephrology], OCHEN. So it's kind of a combined discussion.

Tsan-Yu Hsieh

William Blair & Company L.L.C., Research Division

And one more follow-up, if I may. Obviously, the data was presented at a conference in 2019. Is there any strategy in terms of messaging to kind of [prove] that? And also related to one of the data presentations that you made last year at ASN, I believe one poster was -- talked about if the hemoglobin level beyond 10, you do see kind of a dose response in MACE and hemoglobin. Did this analysis, post versus pre, change that observation?

Mark Eisner

Chief Medical Officer

So first of all, in terms of clarifying prior presentations, in a particular publication of the pooled incident dialysis data that's come out in Kidney International, we are contacting leadership of ASN and the editorial

-- editor, rather, of Kidney International to find the best way forward to provide clarification on those publications and communications. In terms of your specific question, that's not something we specifically looked at yet, but it's part of our overall review.

Operator

And our next question comes from the line of Edwin Zhang with H.C. Wainright.

Xiaodong Zhang

H.C. Wainwright & Co, LLC, Research Division

Sorry, I'm late for the call. I apologize if my questions have been asked. I have two first. For the prespecified stratification factor, is this -- I know this is a new analysis. Is this the one that FDA and the headcount going to use?

Mark Eisner

Chief Medical Officer

So good question. We believe that the prespecified -- the analysis with the prespecified stratification factors is the primary analysis, which should be emphasized when it comes to the analysis of MACE in both NDD and DD populations. That said, it's always been the plan to provide a variety of sensitivity analyses and different approaches to look at the cardiovascular safety data that's supportive. So I do think that the Advisory Committee, during the FDA's review, they will take a totality of the evidence approach that takes a number of different analyses into account. At the end of the day, we do believe that the benefit/risk profile of roxadustat is positive and that the review will likely conclude that.

Xiaodong Zhang

H.C. Wainwright & Co, LLC, Research Division

Okay. I just read through your press release. Looking at the table, I see the incident dialysis. Correct me if I'm wrong. Based on the new analysis, I guess, the superiority we had before in incident dialysis is no longer valid. Is that right?

Enrique A. Conterno

CEO & Director

Yes. Yes, we mentioned that. That is correct. Based on the prespecified stratification factors, we can no longer conclude superiority in that side.

Operator

Thank you. I would now like to turn the call back over to Enrique for any closing remarks.

Enrique A. Conterno

CEO & Director

I want to thank everyone for coming and joining us today at this conference call in such short notice. We remain focused on getting roxadustat through the approval at the FDA and look forward very much to presenting the full data at the Advisory Committee. Thank you very much to everyone for joining. Byebye.

Operator

Ladies and gentlemen, this concludes today's conference call. Thank you for participating, and you may now disconnect.

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Monday, May 10, 2021 9:00 PM GMT

S&P Global Market Intelligence Estimates

	-FQ4 2020-	-FQ1 2021-	-FY 2020-	-FY 2021-
	CONSENSUS	CONSENSUS	CONSENSUS	CONSENSUS
EPS Normalized	(0.19)	(0.91)	(1.65)	(1.57)
Revenue (mm)	100.82	41.84	212.09	388.36

Currency: USD

Consensus as of Apr-20-2021 12:36 PM GMT

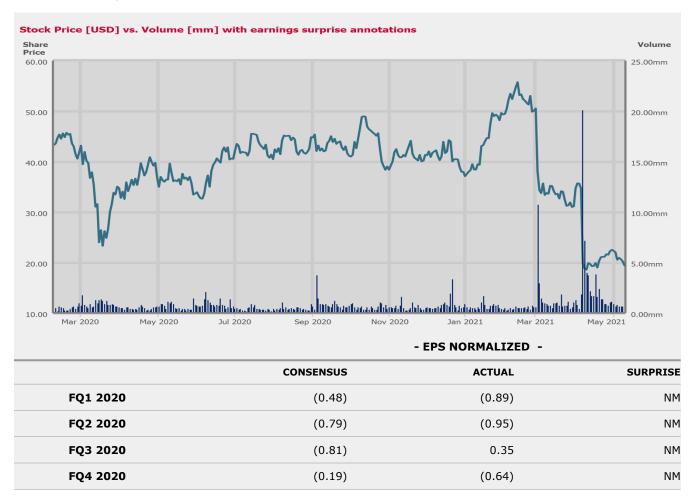


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Presentation

Operator

Good day, and welcome. Thank you for standing by. Welcome to the FibroGen First Quarter 2021 Financial Results Conference Call. [Operator Instructions] Please be advised that today's conference is being recorded. [Operator Instructions] I would now like to hand the conference over to your speaker for today, Mr. Michael Tung. Please go ahead.

Michael Tung

Investor Relations Executive

All right. Thank you, Erica, and good afternoon, everyone, and welcome to FibroGen's conference call for our fiscal 2021 first quarter. I'm Michael Tung, Vice President of Corporate Strategy and Investor Relations at FibroGen.

Joining me on today's call are Enrique Conterno, our Chief Executive Officer; Dr. Percy Carter, our Chief Scientific Officer; Pat Cotroneo, our Chief Financial Officer; Dr. Mark Eisner, our Chief Medical Officer; Thane Wettig, our Chief Commercial Officer; Chris Chung, our Senior Vice President of China Operations; and Dr. Elias Kouchakji, our Senior Vice President of Clinical Development, Drug Safety and Pharmacovigilance. Format for today's call includes prepared remarks from Enrique, after which we will open up the call for Q&A.

I'd like to remind you that remarks made on today's call may include forward-looking statements based on FibroGen's current expectations. Such statements may include, but are not limited to, statements regarding our collaboration with AstraZeneca and Astellas; financial guidance; the initiation, enrollment, design, conduct and results of clinical trials; our regulatory strategies and potential regulatory results; our research and development activities, commercialization and results of operations; risks, plans, market opportunity and strategy related to our business; the planned FDA Advisory Committee meeting and other anticipated FDA interactions; and certain other business matters.

Such forward-looking statements are subject to significant risks and uncertainties that could cause actual results and events to differ materially from those anticipated in such statements. For a discussion of these and other material risks and factors that could affect our future financial results and business, please refer to the disclosure in today's press release reporting our fiscal 2021 first quarter financial results and business update, our most recent Forms 10-K and 10-Q and reports that we may file on Form 8-K with the Securities and Exchange Commission.

All statements are made as of today, May 10, 2021, based on information currently available to us, and FibroGen does not undertake any obligation to update publicly any forward-looking statements whether as a result of new information, future events or otherwise, except as required by law. Today's press release reporting our fiscal 2021 first quarter financial results and business update and a webcast of today's conference call can be found in the Investors section of FibroGen's website at www.fibrogen.com.

With that, I would like to turn the call over to Enrique Conterno, our CEO. Enrique?

Enrique A. Conterno

CEO & Director

Thank you, Mike, and good afternoon, everyone, and welcome to our first quarter 2021 earnings call. Today, I would like to provide a high-level summary of the most important accomplishments and developments in recent months. Pat Cotroneo, our CFO, will then review the financials, after which we will open up the call for your questions.

I reiterate my assessment that FibroGen is uniquely positioned to create significant value for patients and shareholders by executing on the 3 areas of focus as shown on Slide 2: number one, ensuring regulatory and commercial success of roxadustat, a transformational medicine for the treatment of anemia, first, in patients with chronic kidney disease, but with significant potential for expansion to treatment of additional

indications; number two, accelerating the development of pamrevlumab in 3 indications with significant unmet

[Audio Gap]

advanced unresectable pancreatic cancer, Duchenne muscular dystrophy and idiopathic pulmonary fibrosis; and number three is strengthening research productivity by leveraging our leadership position both in hypoxia-inducible factor and connective tissue growth factor biology and by accessing external innovation. Today's call will include a review of roxadustat, our continued strong performance in China and our clinical trial programs.

Let us get started with the roxadustat U.S. New Drug Application, or NDA, review. In March, we announced that the FDA has decided to hold an Advisory Committee meeting for the roxadustat NDA. Our team remains focused on preparing for the upcoming Advisory Committee meeting, which is tentatively scheduled for July 15. In April, we made an announcement clarifying for the FDA and the medical and investment communities certain prior disclosures of primary cardiovascular safety analysis from the roxadustat Phase III program for the treatment of anemia in chronic kidney disease. Our meeting with the FDA was productive, and we have had further productive discussion with them regarding the outcome.

Importantly, this clarification does not impact our overall conclusions regarding the comparability with respect to cardiovascular safety of roxadustat to epoetin alfa in dialysis-dependent patients and to placebo in non-dialysis-dependent patients. As described on April 6, for the incident dialysis subgroup, based on the prespecified stratification factors, roxadustat is comparable but not superior to epoetin alfa with regards to cardiovascular safety. We look forward to publicly discussing the analysis of the cardiovascular safety data at the Advisory Committee in July.

We have reached out to key opinion leaders, primary investigators and medical journals to discuss this matter, and the discussions thus far have been productive and appreciated. We continue to progress our internal review expeditiously, and we'll communicate at the appropriate time. Importantly, we are putting controls in place to prevent this type of occurrence in the future. I want to reiterate that we continue to have confidence in the roxadustat data and in the safety and efficacy profile demonstrated in the Phase III program. FibroGen and AstraZeneca are committed to working together with the FDA to bring roxadustat to patients with anemia CKD in the U.S.

Our pre-commercial activities have continued. FibroGen recently presented additional analysis at the National Kidney Foundation Spring Clinical Meeting and the ISN World Congress of Nephrology, and there continues to be significant interest in roxadustat from the clinical community. Health care professional disease education activities are ongoing and expected to increase through the official launch. Our partner, AstraZeneca, has a comprehensive renal commercial presence in the U.S. and together, we are committed to make roxadustat available to as many CKD patients as quickly as possible.

In order to ensure patient access, AstraZeneca is leading the discussions with dialysis organizations and with payers who cover non-dialysis patients. We have submitted manuscripts covering the CKD anemia Phase III studies to peer-reviewed journals. As noted in Slide 3, 6 of these manuscripts have been published, encompassing both non-dialysis-dependent and dialysis-dependent data, and we expect additional publications of the Phase III data in the coming months.

Astellas recently reported their fiscal year 2020, which ended in the calendar year first quarter. They guided to total Evrenzo sales of approximately \$80 million for the fiscal year 2021, and this guidance includes Evrenzo sales in both Japan and Europe. In Europe, we continue to expect a midyear decision by the European Medicines Agency of the marketing authorization application for roxadustat for the treatment of anemia in adult dialysis and non-dialysis patients with chronic kidney disease.

Moving now to China on Slide 4. We're pleased to report total roxadustat net sales to distributors in China of \$43.5 million for the first quarter versus \$29.2 million in the fourth quarter of 2020. An increase in uptick continues to be driven by both an expansion in hospital listings and broad adoption within listed hospitals. Under the revised partnership structure, FibroGen reported \$15.4 million in China roxadustat net product revenue for the first quarter of 2021.

As we have previously disclosed, beginning the first quarter, a jointly owned distribution entity, or JDE, is responsible for selling roxadustat to distributors and will pay for AstraZeneca's commercialization efforts in China and AZ's portion of the profit share. Previously, FibroGen was responsible for these items. The JDE is expected to account for over 95% of overall China roxadustat sales volume going forward. The rest will continue to be conducted directly by FibroGen.

Hospital listings continue to be a key focus of our launch efforts. Notably, at the end of the first quarter, roxadustat was listed on hospitals that collectively represent approximately 74% of the CKD market opportunity in China. As you can see on Slide 5, interestingly, since the inclusion of roxadustat on the NRDL, the ESA market growth has accelerated. In fact, ESA revenue over the last 6 months have shown 21% growth over the same period of the prior year.

Moving to Slide 6. Roxadustat has expanded the anemia of CKD category over the past 14 months, which translates into roxadustat adding new patients to the anemia of CKD category. Combining this view of roxadustat uptake along with the growing ESA category as shown in the previous slide, it's evident that roxadustat is growing share in an expanded market, which is a great sign. Finally, as shown on Slide 7, roxadustat is the #1 branded treatment for anemia of CKD in China for each of the past 2 months with a 27% value share in the segment that includes all ESA products and roxadustat, currently the only HIF-PHI on the market.

We continue to see significant roxadustat utilization across a range of anemia of CKD patient populations. Approximately 65% of patients treated with roxadustat in China are on dialysis, covering hemodialysis and peritoneal dialysis, while the remaining 35% are not on dialysis. This broad utilization pattern bodes well for long-term success and provides critical learnings as we prepare to launch roxadustat in the U.S., Europe and in other countries. We look forward to keeping you updated as we advance our long-term goal of making roxadustat the standard of care in treating China's CKD anemia patients.

Moving now to our clinical development and starting with roxadustat. During the quarter, we completed enrollment of our Phase II chemotherapy-induced anemia, or CIA, trial. In ASPEN and DENALI, our 2 roxadustat Phase IIIb studies in CKD anemia patients conducted with U.S. dialysis organizations, many patients have transitioned now into the extension phase. We expect to present top line data at a future medical meeting.

Moving now to pamrevlumab. In March, we announced the initiation of LELANTOS-2, a Phase III randomized, double-blind, placebo-controlled trial of pamrevlumab in ambulatory patients with Duchenne muscular dystrophy. Pamrevlumab was recently granted Fast Track designation and Rare Pediatric Disease designation from the U.S. FDA for the treatment of DMD. We value this acknowledgment of the serious and life-threatening manifestations of this rare disease and support of our mission to provide pamrevlumab as a potential treatment option for DMD patients.

I will turn now the call over to our CFO, Pat Cotroneo, for the financial update. Pat?

Pat Cotroneo

Chief Financial Officer

Thank you, Enrique. As announced today, total revenue for the first quarter of 2021 was \$38.4 million as compared to \$24.4 million for the first quarter of 2020. The current quarter revenue consists of \$15.4 million in net product revenue for roxadustat sales in China, \$14.6 million in development revenue and \$8.5 million in drug product revenue for roxadustat bulk drug or active pharmaceutical ingredient.

For the same period, operating costs and expenses were \$108.9 million, and net loss was \$71.8 million or \$0.78 per basic and diluted share as compared to operating costs and expenses of \$105.5 million and a net loss of \$78.3 million or \$0.89 per basic and diluted share for the first quarter last year. Included in operating costs and expenses for the quarter ended March 31, 2021, was an aggregate noncash portion totaling \$25.1 million, of which \$19.4 million was a result of stock-based compensation expense as compared to an aggregate noncash portion of \$22.1 million, of which \$16.9 million was a result of stock-based compensation expense for the same period in the prior year.

At March 31, FibroGen had \$682.6 million in cash, cash equivalents, restricted time deposits, investments and receivables. As mentioned in our last call, we have made some changes in financial reporting. Starting this quarter, the jointly owned distribution entity between AstraZeneca and FibroGen, or the JDE, is responsible for selling roxadustat to distributors and pays for AZ's commercialization efforts in China and AZ's portion of the profit share. Previously, FibroGen was responsible for these items.

As of March 31, the JDE accounted for over 95% of overall China roxadustat sales volume, while the rest continues to be conducted directly by FibroGen. As such, under this new structure, FibroGen reported \$15.4 million in China roxadustat net product revenue for the first quarter of 2021 on a U.S. GAAP basis, which included FibroGen's revenue generated from our sales through the JDE as well as our direct sales in China. To provide context for the operating results of our roxadustat business in China, total roxadustat net sales, including sales through the JDE to its distributors and FibroGen China's direct sales to our distributors, was \$43.5 million for the first quarter of 2021.

Looking ahead at our broader financial picture, we have a total of \$245 million in potential milestones expected by the end of the year for anticipated U.S. and EU approvals and first commercial sale in the U.S. At this point in time, we have no changes in expectations in any of the anticipated milestones between now and year-end 2021. Based on our latest forecast data, we continue to estimate our 2021 ending balance of cash, cash equivalents, restricted time deposits, investments and receivables to be in the range of \$660 million to \$670 million assuming U.S. and EU roxadustat approval in 2021.

Thank you. And now -- I would now like to turn the call back over to Enrique.

Enrique A. Conterno

CEO & Director

In closing, this is an exciting time for FibroGen. Roxadustat continues to perform very well in China and is under regulatory review in the U.S., Europe and other geographies. Our team remains focused on preparing for the upcoming Advisory Committee meeting that is tentatively scheduled for July 15, and we look forward to presenting the roxadustat data in a public forum. Pamrevlumab is our wholly owned potential first-in-class new medicine in Phase III development in 3 indications with significant unmet medical need: locally advanced unresectable pancreatic cancer, Duchenne muscular dystrophy and idiopathic pulmonary fibrosis.

Finally, we continue to advance our research agenda. We're delivering on our unique scientific expertise, strengthening and broadening our internal capabilities, while also looking for external opportunities with the goal of expanding our pipeline of innovative drug candidates. As shown on Slide 8, we're in a strong financial position of roxadustat sales ramp-up with approximately \$682 million in cash and another \$245 million in anticipated roxadustat milestone payments expected during 2021.

I would like to take a moment and also welcome Tricia Stewart, who we recently appointed as Chief People Officer at FibroGen reporting to me. She comes most recently from Genentech and will be responsive for advancing our people and culture strategy. Looking forward, I believe we're positioned for success. Now I would like to turn the call back to the operator for questions. Erica?

Question and Answer

Operator

[Operator Instructions] Our first question comes from the line of Annabel Samimy.

Annabel Eva Samimy

Stifel, Nicolaus & Company, Incorporated, Research Division

I'm not sure if I missed the initial comments, but I was wondering if you could tell us, during the preparations for the AdCom, have you conducted analysis of any of the additional clinical benefits that were published or presented or claimed like reduced RBC transfusion efficacy regarding inflammatory status on hyper responders or better iron utilization? And can you feel comfortable that the data that you presented at those meetings are accurate? And then secondly, you had mentioned some critical learnings in China. Maybe you can highlight what those learnings are for us.

Enrique A. Conterno

CEO & Director

Very good. Let me turn the first -- your first question about roxadustat and the benefit risk profile to our CMO, Chief Medical Officer, Mark Eisner.

Mark Eisner

Chief Medical Officer

Yes. Thanks for the question. So yes, the answer to your question is, yes, we have confirmed the additional benefits in terms of hemoglobin increase from -- with roxadustat, reduction in red blood cell transfusions, roxadustat having benefit in patients with high CRP and who are functionally iron deficient. So we've been able to confirm all of those results, and that has not changed since our April 6 press release.

Enrique A. Conterno

CEO & Director

Very good. Clearly, I think when it comes to China, I think the results in China, I think, I would call nothing short of impressive and quite frankly, gives us a lot of confidence for how roxadustat is becoming a primary choice when it comes to treating anemia of CKD patients in China across the continuum of both DD and NDD. There are a number of learnings that we are capturing from China. One of them, I think I've mentioned in the past, was we've seen a faster-than-expected uptick, in particular, in the NDD segment. And what we basically see is basically also excellent feedback because it is -- when it comes to a launch, clearly, the first few quarters could be always impressive.

But now I think we have a string of quarters where we've seen continued growth quarter-on-quarter that basically reflects not just the overall benefit/risk profile of roxadustat that we've discussed, but also the feedback from health care professionals and patients in terms of what roxadustat is offering in the real world. So I think it's very -- honestly, we are very encouraged with that and the potential read-through of that to other markets.

Operator

Your next guestion comes from the line of Michael Yee.

Michael Jonathan Yee

Jefferies LLC, Research Division

We had 2 questions. The first was to the extent you can talk about maybe topics or relevant areas of interest that you think will be discussed or could be a focus for the panel, that would be great. Since it sounded like you've had good ongoing conversations and things, maybe you could shed some general light on how to think about that from an expectation standpoint. And the second was related, which was

that I know that it is being reviewed in terms of an AdCom from the cardiovascular renal group. Is that a separate group that you've had dialogue with? Or how does that play into things in terms of ongoing discussions?

Enrique A. Conterno

CEO & Director

Yes. I'm going to have Mark Eisner try to answer both of those questions, and I will complement as appropriately. Mark?

Mark Eisner

Chief Medical Officer

Yes. So thanks for the question. So yes, we have been having collaborative dialogue with the FDA about the Advisory Committee. I think both the agency and FibroGen and our partner, AstraZeneca, want to make sure that we have a very fulsome discussion at the Advisory Committee and give the Advisory Committee members the information they need to fully understand the program. In terms of the themes, I think I'd largely characterize it around the benefit/risk profile of roxadustat for patients with CKD anemia and just further explaining the safety and the efficacy of the medicine for NDD and DD populations and getting the input particularly from expert nephrologists who treat patients with CKD anemia. So that's kind of a broad answer, but that's where we are with the agency at the moment.

And in terms of you mentioned that this will be a cardiorenal drug advisory committee, which it is, and yes, we've had conversations both with the office -- at the office level with the cardiorenal -- it's actually [indiscernible] but includes cardio and renal and also with the benign hematology division. So we've had discussions at all those levels of FDA, including the various stakeholders for both disease areas.

Enrique A. Conterno

CEO & Director

Yes. I would just maybe add that I think our preparations when it comes to the AdCom, I think, are progressing well.

Michael Jonathan Yee

Jefferies LLC, Research Division

The reason I ask is because this is -- supposedly, we'll have renal or nephrology experts on there and you think that, that would be a positive, yes, because there would actually be experts on the panel rather than just people who are not familiar with that. Is that a fair statement?

Mark Eisner

Chief Medical Officer

I think it is important to have nephrology experts with the -- which I believe the FDA intends to have because they do treat patients with CKD anemia both in the NDD setting and dialysis setting. So they're in a very good position to understand the unique attributes of roxadustat and where the benefit/risk is going to be positive. So yes, I think it's going to be really important to have that nephrology input.

Operator

Your next question comes from the line of Edwin Zhang.

Xiaodong Zhang

H.C. Wainwright & Co, LLC, Research Division

First one, can you please remind us the purpose and design of the ASPEN and DENALI clinical trials? How are the new study results going to affect or help the adoption of roxadustat in the U.S. dialysis organizations? And then I have a follow-up.

Mark Eisner

Chief Medical Officer

Sure. So the and ASPEN and DENALI trials, they're single-arm, open-label studies conducting -- conducted in large dialysis organizations that, I think, will provide an understanding of roxadustat in a more real-world clinical setting. It is a clinical trial, but it is one that's conducted in a setting that's very much a real-world clinical setting for hemodialysis patients. We are expecting to present data sometime by the end of the year in a scientific meeting. And for the [other] large dialysis organizations, I mean, the data, we are committed to making that available to them at their request so they can further understand the value and the use of roxadustat in their patient populations.

Xiaodong Zhang

H.C. Wainwright & Co, LLC, Research Division

Okay. My next question on pamrevlumab on DMD. Are we going to expect a publication of the Phase II study, including the 2-year data? And what's your current thinking on the market opportunity of pamrevlumab in DMD?

Enrique A. Conterno

CEO & Director

Yes. We'll have Mark answer the question on pamrevlumab, Duchenne muscular dystrophy and questions, in particular, around the 2-year data on publishing the data.

Mark Eisner

Chief Medical Officer

Right. So we are in the process of working to get the 2-year outcomes data published. So I don't have a specific date for you yet, but we're working on that actively. And we do think that's important to show how the benefits continue to be between year 1 and year 2.

Enrique A. Conterno

CEO & Director

And I think you were asking about the overall opportunity in DMD, and maybe let me try to frame that in the context of the 3 programs that we basically have for pamrevlumab. We see each one of these opportunities, whether it's IPF, LAPC or DMD, as significant opportunities. The IPF opportunity, when we look at from a -- clearly, I think it's important to say that the 3 of them are significant unmet clinical needs. The IPF opportunity is expected to be larger than the other 2, LAPC then and then DMD. But each one of those opportunities is significant on its own, and collectively, I think they do represent a massive opportunity. We are -- we expect that we will have the LAPC results and DMD results in the second half of next year from a readout perspective. While in the case of IPF, we have not shared that, but we expect to share at a specific time in the near future.

Operator

Your next question comes from the line of Jason Gerberry.

Jason Matthew Gerberry

BofA Securities, Research Division

I guess just first on the slew of shareholder suits, can you just remind us sort of what's the burden of proof in these matters? I would assume the fact that the FDA is moving forward with an AdCom inherently implies there's some ambiguity around the safety and the upper bounds of the confidence interval on NDD. But just kind of curious if you can just provide a little bit of a helpful legal framework to think about the shareholder class-action suits.

And then my second question is just on DD. Assuming approval, what I wonder about is as the second and third HIFs come to market, what are your thoughts that the dialysis organizations might look to hop from one product ending at [indiscernible] phase and some of the financial benefits to the second and subsequent third products that may offer some of those financial benefits? Just thinking about the longevity of a dialysis launch.

Enrique A. Conterno

CEO & Director

Yes. Thank you. I think on your first question, we do not comment on either ongoing or potential litigation. That's -- as far as your question about HIFs and how would the second or third HIF, whenever it comes, impact the contracting or maybe a dialysis organization being able to move from one HIF to the other, a couple of comments that I would make. First is, clearly, launching first is important, and we've seen that across many different launches across different therapeutic classes because you tend to establish yourself as basically the go-to product, the product that the health care professionals have experience with.

And then second, I think quite frankly, there's no real experience in terms -- or studies showing basically switches from one HIF to the other and who can say that that's going to work well. Keep in mind that our -- at the end of the day, we have to look at also the clinical data and how do the products basically compare overall. So there are a number of variables. And I don't believe this is -- that we should be thinking -- as we've seen in other therapeutic classes that it's either appropriate or that it will be convenient to just basically switch products [in large] from one compound to a different one or the same class. I think there are a lot of considerations that would have to be made.

Operator

Your next question comes from the line of Geoffrey Porges.

Geoffrey Craig Porges

SVB Leerink LLC, Research Division

First one, I'll ask a couple that you probably [kind of wouldn't] answer and then one that hopefully you can. The first is in the discussions with the FDA, can you give us a sense of whether the basis for the labeling discussions is going to be the protocol stratification or the [post tox] stratification? That would be helpful.

And then secondly, you have these Phase II and Phase III studies in CIA and MDS coming in the second half of the year and the beginning of next year. And then obviously, those indications are completely different price points to the dialysis and non-dialysis indications where, of course, you have to think about the bundled rate and all that sort of thing. So have you had any further thoughts, Enrique, about whether you will price differentially for the different markets and whether that's feasible, or whether we should expect you to price pretty much in the same band?

And then lastly for China. Is the reported revenue under the new arrangement that comes into your results as a proportion of the total revenue in market, is that percentage likely to remain relatively constant going forward or actually increase? Or is it just going to be really bouncy?

Enrique A. Conterno

CEO & Director

Yes. Thank you, Geoff, for your questions. Let me first say that when it comes to our interaction with the FDA, I think we're not really providing any detail when it comes to our interactions. Clearly, just in general, I think the -- we expect that the FDA will be looking at the overall evidence, what we -- including what the primary analysis is and also a number of sensitivities around some of those analysis. So far, we feel good about our discussions with the FDA in that they are very productive discussions.

In terms of your question around CIA and MDS, clearly, when it comes to MDS, I think that's where the biggest price differential is. It's also in CIA. But of course, we're going to need to see when it comes to CIA what, based on the Phase II results, what is the dose and so forth and what also -- what is it that we're basically seeing. So I expect that CIA, while there might be some slightly different price points, I don't view them as meaningful. In the case of MDS, there is a pretty significant difference between products in the markets that have been used for MDS and basically what we would price, for example, anemia of CKD with roxadustat.

I think it's fair that we want to make sure that we are appropriately pricing so that we can -- based on the value that the product and the medicine is offering in the different populations. And while that is

always the goal, we all know that, that is a challenge, in particular, in -- it's a challenge in the U.S. how to effectively do that. So at this point in time, we're not commenting on how we are thinking about that. But clearly, that has to be part of our strategic thinking just to ensure that we are appropriately receiving the value for what roxadustat is offering in the different patient populations.

Finally, you asked a question about the relative -- FibroGen reported revenue relative to the overall sales -- net sales to distributors between the joint distribution entity and FibroGen's direct sales. And with that proportion that we reported this quarter, that is going to be the ongoing proportion going forward. There are a number of factors that play into this. We provided some guidance, I think, during the last earnings call that we expected that number will be somewhere between 30% and 45%. We need to -- I -- we continue with that type of guidance. So I think it's going to bounce a little bit based on a number of different considerations. I think the bottom line here is when we look at the overall net sales of roxadustat to distributors, it is pretty clear, I think, that the product is having an incredible performance and is really valued, I think, in terms of what it's offering patients in China.

Operator

The next question comes from the line of Yaron Werber.

Brendan Mychal Smith

Cowen and Company, LLC, Research Division

This is Brendan on for Yaron. Just a couple of quick ones from us. I think, first, looking at the growth of roxadustat sales in China, it kind of looks like January and February sales are maybe more or less flattish. Are there some specific drivers behind that, that you can maybe identify to help us understand just some of the commercial dynamics at play there?

And then secondly, just on the DENALI and ASPEN studies, I think you mentioned just now that we could get data from there maybe by the end of this year. If memory serves me, I think we were supposed to see that data in Q1 of this year originally. So I guess, have there been any delays in enrollment or treatment there that you might be able to comment on?

Enrique A. Conterno

CEO & Director

Yes. Okay. Let me try to address your question about China. And I think you mentioned that the sales in China maybe were -- if I understood correctly, you felt they were flattish in January and February. I don't think that's the case for roxadustat. Clearly, we're basically seeing increased share, and we're seeing increased share in a growing market, right? So we feel very good about where we are. And when we look at our internal sales in the first quarter, clearly -- or the sales that we reported just right now [what is] overall net sales to distributors, I think we've seen a significant increase north of 40% sequentially between Q4 and -- of 2020 and Q1 of 2021. So I don't believe that's the case. And your second question was related to DENALI and ASPEN, and I'm going to have Mark Eisner provide an answer.

Mark Eisner

Chief Medical Officer

Yes. I think that there are 2 different things. One is when -- I mean, as this is an open-label study, it's potentially possible to provide for dialysis organizations data cuts for their own use. So that was, starting Q1, possible. What I was talking about as a distinctive factor was when we expect top line data from the overall study to be available, that -- I think we've been consistent that, that should be by end of year at a medical meeting.

Operator

Your next question comes from the line of Difei Yang.

Difei Yang

Mizuho Securities USA LLC, Research Division

Just 2 questions, circling back to the DENALI and ASPEN trials. Would you be able to clarify if the sites -- the clinical sites are mostly DaVita or Fresenius or is a balance of the 2? And the second question is related to AdCom. So what's the role for AstraZeneca for this AdCom? Is it primarily driven by FibroGen?

Enrique A. Conterno

CEO & Director

Yes. Let me -- just very quickly on DENALI and ASPEN. We're not commenting on who are we doing those studies with. But as we said, it's -- clearly, we're doing this with large dialysis organizations. And as far as the AdCom, of course, FibroGen is the sponsor. So we're the sponsor of the NDA. And maybe, Mark, you can provide some additional comments on the role of AstraZeneca.

Mark Eisner

Chief Medical Officer

Yes. I would describe it as a highly collaborative effort between FibroGen and AstraZeneca. We've essentially formed a joint working team to prepare for the Advisory Committee, to prepare the presentations and get ready for the Q&A. So it's a highly collaborative process between both companies.

Operator

Your next question comes from the line of Paul Choi.

Aliza Bram Seidenfeld

Goldman Sachs Group, Inc., Research Division

This is Aliza on for Paul. A quick one from us. Now that pamrevlumab has Fast Track and Rare Pediatric Disease designation for its DMD program, can you walk us through how you're thinking about any update in timing in this program, regulatory and potentially commercial as well?

Enrique A. Conterno

CEO & Director

Yes. Maybe I will comment on -- I'll make some initial comments, and Mark will add some additional color. Clearly, I think the key for us when it comes to ensuring that we can complete our DMD and be able to bring this medicine to patients is really the enrollment of our trial. So we are working very closely to -- and diligently to try to ensure that the enrollment in DMD for both of our trials can happen as quickly as possible. To that end, we've added a number of additional sites, including now in China where we have gotten the approval, and we started basically recruiting patients in DMD as well that will contribute to the overall global program.

So we are excited about those designations. I think the designations generally basically allow for basically more interaction with the FDA in this particular case related to this program. And I think that's a benefit from a regulatory review process and can provide the basis to be able to move quickly -- more quickly and/or resolve any type of issues in a broad manner. Mark, any additional comments?

Mark Eisner

Chief Medical Officer

No. I think that was well stated, Enrique. I mean, I would say that both the Fast Track and the pediatric rare disease designation from FDA speak to the high unmet medical need and the potential of pamrevlumab to help patients with better outcomes with this high unmet medical need. I think it helps us in terms of enrolling the trial because it's just another way of highlighting how important these studies are. So overall, I think it's a real positive for our ability to enroll these trials and to focus on doing it expeditiously.

Operator

The next question that we have is from the line of Andy Hsieh.

Tsan-Yu Hsieh

William Blair & Company L.L.C., Research Division

Great. So I have 2 questions regarding the China market dynamics, maybe for Chris. So the trajectory in terms of hospitals, it seems, has been very impressive. So I'm just curious, as you kind of reach -- going from about 74% to 80% to 90% [to] high 90%, what are some drivers that your team is thinking about in terms of continuing to grow that revenue line? And also, in terms of the kind of the periodicity of the national reimbursement dynamic, I think every single year, there is kind of scheduled pricing cuts mandated by the government. I'm just wondering what the FibroGen China team is thinking about in terms of kind of preparing for that.

Enrique A. Conterno

CEO & Director

Yes. I think I'll have Chris indeed address both questions when it comes to drivers for revenue growth going forward. In China, we tend to have increased -- there's a limit to given how well we've done with hospital listings in terms of how much will that continue to contribute. And then also, I think you may have a question about the NRDL. And I would say the negotiation for products happens every 2 years, not every year, although there's -- every year, there's some product that will be negotiated. Chris?

Christine L. Chung

Senior Vice President of China Operations

Sure. So to answer the first question, we think of hospital listings as market access. So until you're listed in a hospital formulary, no physician can dispense. So once you get your foot in the door, in this case, roxadustat, you still need to convert the prescribers one at a time. So let's say there are 35 nephrologists in the department. You don't get all 35 in the first day. You might get 5. The next year, you might get 10, and hopefully, there's an upward trajectory. And for every single prescriber, let's say, they have 200 patients, you also don't get the 200 on the first day. You might get 20, and then you might get 25%. You might get [50%].

Obviously, if we were successful, we'd love to get the vast majority of prescribers and the vast majority of their patients, but there's some art to new trajectory. So we see getting our foot to the door in terms of the success we have in hospital listings to bode very, very well for future adoption. But really, we are at the very, very beginning of market adoption of roxadustat. So 74% is very good, which means that 74% of the potential market could actually get access to prescriptions, but that doesn't mean that, that's the end of the uptake. I hope that makes sense.

The second question with regards to NRDL. Enrique is absolutely correct. It's renewed every single 2 years. So roxadustat will be up for price negotiations in Q4 of 2021, and the new price will become effective in 2022. There are obviously a number of factors that they would consider in the price: first is the budget impact of roxadustat on the national health care budget; the second, the value proposition of how much we actually save in health care costs and many other factors in the value proposition; and third is really how strong is the market adoption and how much prescribers value this drug. We remain confident in the outcome of price negotiations.

To be clear, if the price only goes in one way, it always goes down. It never goes up. So it's the discretion of the NRDL in terms of how they value it and how much it comes down. Every single year, they come up with a different set of criteria for determining pricing. The 2019 one was different from 2020. The 2021 eligibility criteria and prioritization has not yet been announced. We're working very closely with market access at AstraZeneca to demonstrate the value of our drugs, and we remain confident about a very good outcome in Q4 this year for the price that will be effective for 2 years thereafter.

Thane Wettig

Chief Commercial Officer

Chris, this is Thane. If I could just maybe piggyback on to your answer on the China trajectory to answer and to provide some more color on Andy's first question. This is really the first time we've provided some granularity around China performance over and above revenue and then snapshots of hospital listings and things of that nature. And so if you take a look at some of the slides that we provided, the first

thing to reiterate is that we've got a market that when you add the ESA growth on top of the category expanding nature of roxadustat, it's a market that's really taken off, which really highlights the commercial responsiveness to this category.

And then when you take a look at the market share perspective we've provided, which is a value-based market share of 27%, we're in the process of turning that value-based market share into a volume-based share calculation, which is a bit difficult given some of the dosing dynamics associated with ESAs. But it's probably fair to say that our current volume penetration is much, much lower than 27%, which just speaks to the significant upside potential that roxadustat continues to have in the China market. And we think it's also -- as Enrique said in his prepared comments, it's a really nice read-through to the other markets when we are able to launch in the U.S. and Europe.

Operator

There are no further questions at this time. I would like to turn the call back to Enrique. Please go ahead,

Enrique A. Conterno

CEO & Director

Very good. Thank you, Erica. We very much appreciate everyone's participation in today's investor call and your interest in FibroGen. Please follow up with our Investor Relations team if you have any questions we have not addressed on the call, and enjoy the rest of your day. Thank you very much.

Operator

This concludes today's conference call. Thank you all for joining. You may now disconnect.

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EXHIBIT SS

S&P Global
Market Intelligence

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Thursday, May 13, 2021 10:00 PM GMT

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EXECUTIVES

Enrique A. Conterno *CEO & Director*

ANALYSTS

Jason Matthew Gerberry *BofA Securities, Research Division*

Presentation

Jason Matthew Gerberry

BofA Securities, Research Division

Good evening, everybody, and thanks for joining us at the Bank of America Annual Healthcare Conference being conducted virtually this year. Hopefully, next year -- the CDC just gave us the mask-free mandate. So hopefully, next year, we'll be able to do this in Las Vegas.

This is our final fireside chat of a 3-day event, and I'm pleased to be introducing our next company presenter, FibroGen and CEO Enrique Conterno. So Enrique, thanks for joining us.

Enrique A. Conterno

CEO & Director

Jason, thank you very much for the invitation. I'm looking forward to the chat.

Question and Answer

Jason Matthew Gerberry

BofA Securities, Research Division

Yes. Maybe just kicking things off, maybe just talk a little bit about what drew you to FibroGen. You're coming from Eli Lilly, intimately involved in diabetes, large markets, the primary asset, roxadustat also being something that could be used in pretty large markets. And just overall, what drew you to the company?

Enrique A. Conterno

CEO & Director

Well, I think it's the opportunity to work on transformational medicines. And clearly, it's unique for a company the size of FibroGen to have 2 assets in late stage in both roxadustat and pamrevlumab. And then the ability to be able to bring more products into the clinic. So I think it's exciting, I think, just to think about all the possibilities.

And clearly, I think when we think about roxa, when we think about pam, not just 2 new medicines, but truly 2 medicines can be quite transformational and truly first in class. So quite unique, and I feel that my experience was a really good fit for the company.

Jason Matthew Gerberry

BofA Securities, Research Division

Okay. Maybe we'll talk a little bit about roxa and the potential role that it could play in the dialysis setting, both dialysis and non-dialysis dependent. We could talk about -- a little bit about some of the unique assets of the U.S. market, which hopefully you'll be able to bring that medicine to market. Well, we can get in the time line considerations and then maybe some of the vagaries of what's going on with FDA.

But maybe we'd just set the table for this medicine, which nobody really denies the efficacy benefit that it can provide. It's orally dosed. It has benefits -- unique benefits in certain patients like hyporesponders. So maybe just how do you think about this kind of medicine in the key indications that you're pursuing relative to standard of care, which is an ESA in dialysis, and in non-dialysis, there really isn't a standard of care?

Enrique A. Conterno

CEO & Director

Yes. Clearly, I think it's a pretty significant unmet clinical need when we look at anemia of chronic kidney disease and the opportunity to have a product -- an oral product like roxadustat basically with the type of data that we shared both on DD as well as NDD.

When it comes to DD, as you well said, we have a standard today, which are ESAs that are widely used for people that are on dialysis for the correction and maintenance of hemoglobin, people who have anemia. So it's an important -- it's clearly a very important segment that most of these patients are being treated. Of course, the data that we're -- that we've been most excited about has been the incident dialysis data.

And just to remind everyone, I think when we look at roxadustat, we view it as comparable on both dialysis dependent on non-dialysis dependent, comparable to ESAs on dialysis dependent and to placebo on non-dialysis dependent. And we have now, I think, the opportunity to -- so patients are starting those treatment with dialysis to be able to treat anemia. And we think that roxadustat can be an ideal choice there given the strength of our data and particularly incident dialysis.

When it comes to some additional opportunities, you well pointed out that there are a number of patients that are hyporesponders. We estimate those to be -- to ESAs, we estimate that segment to be as high as 20% of the overall patients on dialysis.

When it comes to NDD, we basically have few patients being treated. In fact, when we look at the 12 months prior to initiation in dialysis, we see that only about 14% of those patients are treated with an ESA. So clearly, a pretty significant opportunity to increase those treatment rates. And clearly, the benefit of that is to try to avoid transfusion, minimize the risk of transfusions.

We are working very closely right now, very diligently to prepare for the Advisory Committee that we -- that has been tentatively scheduled for July 15. I'm excited about the opportunity to share data publicly, quite frankly.

Finally, I think it's important to maybe mention, maybe I'm sounding a bit optimistic, but I am given what I've seen what the product can do. And we can talk about China in a bit. Particularly, the performance in China, I think, is a perfect example of what the transformational product could do. Clearly, the adoption that we're seeing by hospitals, physicians, the feedback from patients, I think, is outstanding. And it's been reflected, I think, on the results that we see.

Jason Matthew Gerberry

BofA Securities, Research Division

Great. You guys have these Phase IIIb trials that are being conducted with dialysis organizations. Can you just remind me what's the status of those trials? Will that -- oftentimes, when new medicines come around, they may help investigators get more experience outside of the rigid trial context, right? Can I switch a patient? How easy is it to switch a patient? Which patients do I feel most comfortable with in terms of utilization of the medication? So maybe just a little context for initiating those trials with large DOs? And what do you think that will help accomplish when you are ready to get to market?

Enrique A. Conterno

CEO & Director

Well, I think those -- first, I think those studies are Phase IIIb studies, and they are important because we are looking at roxadustat in a real-world setting with those large dialysis organizations. Those trials are now fully enrolled. And in fact, some patients have already gone into the extension phase. And we look forward to sharing that data, I think, at a future scientific meeting. Of course, the data will be available to the large dialysis organizations for them to be able to see, I think, the benefits of roxadustat in those specific settings.

Jason Matthew Gerberry

BofA Securities, Research Division

So you -- presumably, with the dialysis approval, you have a TDAPA reimbursement. We've now seen very limited analogs. The analogs that we have seen is basically Amgen's Parsabiv and not necessarily apples-to-apples with what you'd be dealing with because there's not a generic alternative to what you have. It's a biosimilar alternative efficacy-wise.

And so I guess I wonder ultimately if you can speak to some of the practice -- or dialysis organization economic considerations. I realize that your medicine offers much more than an economic benefit to practices. But just how organizations will navigate that because arguably under TDAPA, there's less of a burden on the practice financially to experiment with the new novel medication.

Enrique A. Conterno

CEO & Director

Yes. No, I -- thank you for your question. Clearly, as you well highlighted, I think we really start with the clinical benefits that roxadustat has when it comes to patients on dialysis. And we discussed 2 specific types of patients, patients that are starting dialysis or patients maybe that are hyporesponsive, as very specific patients with roxa can have some of the largest benefits.

But when we think about some of the access, maybe frameworks that are utilized in this particular case, we believe that roxadustat will be eligible for TDAPA. So we intend to basically request TDAPA reimbursement be eligible for that. TDAPA is basically payment adjustments for products that otherwise

would be on the renal bundle. And it's designed -- TDAPA is designed to basically foster and incentivate innovation by basically providing this payment adjustment or additional payment.

Importantly, the considerations here are that the dialysis organization would receive an additional payment when using roxadustat. Of course, this needs to be approved by CMS, and we're working to -- as soon as we get approved, we're going to be working to ensure that we are prepared to make that submission to CMS so that we can get the eligibility as soon as possible.

Jason Matthew Gerberry

BofA Securities, Research Division

Got it. So the interesting thing, I guess, is Amgen, the way that the bundle adjusted post Parsabiv, like they're down 50%, or they're pointing down 50% in terms of their sales level coming out of the TDAPA phase. I mean some of that's just driven, I guess, by the volume pressure. Once that TDAPA phase ended, a lot of maybe DOs went to Sensipar -- generic Sensipar because -- but ultimately, I think part of that, too, is that the bundle didn't adjust to address the Parsabiv pricing level.

Now I guess how do you see that situation evolving for roxa? On the one hand, you could argue we're different. Maybe your product's more innovative. But there's an ESA there. And so maybe the bundled payment allotted for ESAs represents maybe a good benchmark for where your net reimbursement level may come in kind of post TDAPA.

Enrique A. Conterno

CEO & Director

Yes. I think the concept of TDAPA when it comes to trying to foster innovation within the [dialysis] protocols is to ensure that as we think about those 2 years where those TDAPA payments would exist -- and by the way, that's -- we -- that's the current framework basically, TDAPA will last for 2 years. During that time, CMS will basically be assessing the product to determine how the products will be treated now within the bundle, right? And that assessment has to be based on the utilization of the product but also the benefits that they see with the product relative to not utilizing the product.

So I think it's -- at the end of the day, I think the world post TDAPA would be governed by how well did roxadustat perform within the 2-year period as assessed by CMS. I'm quite confident on what roxadustat can deliver. So this bundle, I think it's difficult to say what would be this bundle post TDAPA. But I think it's good to think about the formal assessment that is done and then basically ensuring that these payments are now basically taking some of the benefits that we're seeing into account. Otherwise, if they don't do that, at the end of the day, you're providing only a temporary benefit or economic incentive. But if the clinical benefits are there, I think they need to be rewarded as well.

Jason Matthew Gerberry

BofA Securities, Research Division

Okay. Now NDD is an interesting market. It's very sizable. It -- from what we hear from physicians, one of the reasons why ESAs are underutilized is because of the restrictive hemoglobin targets. What we hear oftentimes is they've got a lot of patients whose hemoglobin levels are around 9, 9.5, can treat to 10. It doesn't make any sense to maybe even start because the hemoglobin thresholds are so restrictive.

Your trial protocol allows for more flexible hemoglobin targets. So just typically, when drugs are given the green light to be studied in a certain way by FDA, they're labeled according to study. So maybe if you can speak to that dynamic and your confidence level that the FDA is comfortable with treating the higher hemoglobin levels. Because it seems like it's an important variable, ultimately from our perspective, to really unlocking the value and getting these patients anemia medication.

Enrique A. Conterno

CEO & Director

Yes. Yes. So clearly, when we looked at our trials, as you point out, I think the hemoglobin target level was 11 plus/minus 1 with roxadustat. We -- as you know, we don't comment on our interaction with the FDA

or try to speculate on what the label will look like. But clearly, I think the results that we've discussed are based on protocols that basically look at those specific targets.

One thing to keep in mind, and I think I'm reflecting on what we basically are learning from China as we think about the NDD market and some of the dynamics there, it is pretty clear that we might be underestimating the long-term opportunity when it comes to building that market in NDD. I think we've said for quite some time that we expect that the uptake when we look at the dialysis setting will be fast, and maybe a higher proportion of the overall patients will be dialysis-dependent patients relative to vis-a-vis NDD but that over time, we expect the NDD opportunity to scale to be much larger, significantly larger than the DD opportunity.

And what we basically see in China is exactly that. It's -- in China right now, I think it's 1/3 of the patients -- or 35% of the patients today are patients in the NDD setting and 65% DD. But what's more interesting is to look at the dynamics of the overall market, which may seem a little bit counterintuitive because since roxadustat was launched in China, what we've seen is actually the ESA market accelerate. So not just continue to expand. It is continuing to expand, but it's actually expanding faster than it was prior to the roxadustat launch.

That is pretty unusual, and it speaks to a pretty unmet need. And now that we are, together with AstraZeneca, commercializing the product and -- in China. But also talking about anemia, the importance of treating anemia, not just in the DD setting but in the NDD setting, I think what is -- basically it's making the category for anemia significantly larger. So this type of trend that I'm describing is -- and these types of trends tend to last not just for quarters, but these tend to be trends that basically play out over years. So I'm extremely encouraged by what we see there.

And I think the one thing that we maybe underappreciated, in addition to all the clinical benefits, because sometimes we tend to be quite scientific, but it's -- the fact that this product is an oral product. And as we know with ESAs, basically patients have to go into a physician office to have the product administered. That will certainly happen. That's the practice here in the U.S. So the fact that it's an oral product, I think, provides a different level of maybe also convenience in addition to some of the clinical benefits.

So you have the importance of treating anemia and avoiding or minimizing the risk of transfusions. But then in addition to that, we look at some of the specific benefits of roxadustat, and we add to that the fact that it's an oral product, and I think it makes the opportunity significantly larger maybe than we initially saw.

Now of course, I am translating China into other markets. And I think for the most part, I think it's a fair assessment outside of access because access to the product tends to vary and be very specific from market to market. But outside of access, I feel like physician adoption, we can -- there's a lot of learning that we can take from China, and that has to been pretty encouraging.

Jason Matthew Gerberry

BofA Securities, Research Division

Right. And I mean I guess, we, as drug analysts, are very -- oftentimes end up being very U.S.-centric. And typically, when a new major launch hits a category, it kind of grows the broader category and other drug categories benefit from that. So do you think -- if you had to come up with a hypothesis in terms of what's going on there, what's driving that ESA utilization, is it more or less doctors are now starting to just treat more and having to go to other options as well?

Enrique A. Conterno

CEO & Director

Yes. Clearly, our -- this is something that we are studying. But I think what -- this is my view. What we're seeing is basically additional treatments, in particular, so increasing the treatment rate, in particular, in the NDD market. And that increase is so significant. The -- not only is roxadustat growing very fast. As you know, we basically had \$43.5 million in Q1 in net sales to distributors. That's an increase vis-a-vis the 29-plus that we had in Q4 of 2020, so very -- a good sequential growth.

So yes, it's pretty interesting to see, I think, what's happening. And I think it's all about -- it's been largely driven by increases in the treatment rate in NDD. And I think that bodes extremely well for the future.

Jason Matthew Gerberry

BofA Securities, Research Division

Yes. So you've put some rough guidance parameters around the revenue opportunity for roxa in China. I think greater than \$500 million based on the guidance that's out there. You seemingly have gotten coverage in hospital setting or for the dialysis center setting much faster than I think you would have expected. So maybe what's next? What are the future catalysts? Or is it just kind of an execution story going forward in that market?

Enrique A. Conterno

CEO & Director

Yes. It is an execution story. Keep in mind that we don't expect another HIF-PHI in China for some time. And as you well said, our -- we now basically have access to about 74% of the overall CKD anemia opportunity in China. And that's going to continue to increase.

What are some of the additional drivers of growth? It is about basically continuing the adoption cycle. So we will see increased adoption in hospital where we're listed. What's the concept there and why do I feel highly confident is we basically have much higher share in incident dialysis, which in a certain way, those patients tend to carry through and become patients that are on prevalent dialysis. So over time, we -- that incident dialysis will basically be reflective of the overall share that we have in the dialysis setting. So it is a matter of continuing to execute our strategy. There's additional opportunity for increased listing, but really, I think the big opportunity is going to be on both the adoption but also on the adherence, making sure that the length of therapy is appropriate so the patient can get the full benefit.

And yes, we've guided to peak sales of north of \$0.5 billion for roxadustat in China for CKD anemia. So for us, it's basically executing our strategy. Keep in mind that we have additional opportunities, indications in China. We are pursuing both MDS, CIA also in China. So chemo-induced anemia and myelodysplastic syndromes. Those indications are above and beyond the guidance that we have provided.

Jason Matthew Gerberry

BofA Securities, Research Division

Yes. Okay. Maybe just shifting to the U.S. market opportunity and regulatory situation in terms of -- so it sounds like this is a joint collaborative effort in terms of your preparations and getting ready for the advisory panel. Maybe just talk about how helpful it is to have AstraZeneca as a partner here in terms of navigating the upcoming regulatory outcome.

Enrique A. Conterno

CEO & Director

Yes. Clearly, for us, I think a critical job is going to be our preparation for the Advisory Committee to be held on July 15. To do that, I think you probably know there's a -- given all the learning, there's a -- we've put together a really good process to ensure that we're going to be as prepared as we can be. That includes anything from doing mock reviews, mock outcomes and so forth.

But importantly, too, is I think it's key that we work -- continue to work collaboratively with the FDA to allow the Advisory Committee to have the best assessment of the product so that they can appropriately advise. I feel very strongly about this. And I feel that our preparation is giving me additional confidence in terms of what I expect will be a very productive and positive discussion at the AdCom on July 15.

Jason Matthew Gerberry

BofA Securities, Research Division

You gave a little bit of a preview, I think, on the last earnings call. Yes. It seems kind of obvious in the sense when you have these therapies that are undeniably effective, right, in categories like this that the

focus tends to be just around a vote around views on safety and risk/benefit. But wondering if there's any other additional commentary you want to offer there.

Enrique A. Conterno

CEO & Director

No. I think at the -- when it comes to an Advisory Committee, clearly, you're bringing relevant experts to provide perspective, advice to the FDA. And risk/benefit, the benefit/risk is always part of that discussion. Clearly, I think when it comes to the efficacy, I'm sure that it would also be discussed. But I think with roxadustat, it's pretty clear, very consistent and consistent across many different patient types, including patients that have inflammation and so forth.

And the -- when we look at our data, we have a number of different trials, both in DD and NDD. And then we need to look at the overall cardiovascular profile. And as I mentioned, we see our profile being, when it comes to MACE, noninferior to ESAs on DD and non-inferior comparable to placebo on NDD.

The -- so at this point in time, of course, the FDA will look at the primary analysis, but I'm sure we will also do a number of additional sensitivity analysis and we -- that I'm sure will be discussed. Those sensitivity analysis, in some cases, look -- make the product -- or hazard ratios lower, in some cases, higher. But all in all, I think should help understand, I think, the overall profile of the product better. And I'm optimistic about -- given our preparation that we will have a good [showing].

Jason Matthew Gerberry

BofA Securities, Research Division

Yes. It seems to me the key challenge is the managing the magnitude of complexity for the panelists given the different studies, the different analyses and how you can have a focused discussion. We know sometimes advisory panels can sometimes -- there can be some confusion just given the quantums of data involved.

Enrique A. Conterno

CEO & Director

Yes. And I think it's probably important to reflect of what makes -- well, there are a number of factors, what factors can we influence appropriately to make sure that we can have a productive discussion at the AdCom. And as part of that, of course, our preparation is part of that. But also, I think to the collaboration with the FDA and making sure that all the analyses are truly informative, I think, could be important as well. So it's -- data is coming soon, and we're looking forward to it.

Jason Matthew Gerberry

BofA Securities, Research Division

Yes. So are we. So I guess just a final question because we're almost out of our time. But pamrevlumab, IPF, maybe if you can just comment how -- you got some dynamics going on, I assume, with the enrollment. You have COVID, but you also have a competitor who wind down their IPF trial, large IPF trial. Maybe that might be a tailwind for enrollment. Just any color you can provide on that process.

Enrique A. Conterno

CEO & Director

Yes. Two things. First, when it comes to pamrevlumab, the first readout that we will see are in LAPC, locally advanced unresectable pancreatic cancer, and DMD, Duchenne muscular dystrophy. And we have basically guided towards a readout in the second half of next year for those 2 important indications.

When it comes to IPF, you're right. I think both COVID, the fact that we are seeing basically less cases of COVID, but in addition, the fact that one of the product that was being studied for IPF recently stopped their trial. Both of those, I think, are helping our involvement. We do have additional sites as a result of that, that are now basically enrolling pamrevlumab. And also on sites that maybe we're enrolling both trials, now we have additional patients, patients that basically can come into our study. So I think the

dynamics, I think, when it comes to enrollment have been getting more positive than what they have been.

Jason Matthew Gerberry

BofA Securities, Research Division

All right. Well, great. Well, Enrique, thanks so much for your time and best of luck here in the coming milestones for the company.

Enrique A. Conterno

CEO & Director

Jason, thank you very much for the time, and congratulations on a successful conference.

Jason Matthew Gerberry

BofA Securities, Research Division
Thank you. All right. Operator, with that...

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FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

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EXECUTIVES

Enrique A. Conterno CEO & Director

ANALYSTS

Michael Jonathan Yee Jefferies LLC, Research Division

Presentation

Michael Jonathan Yee

Jefferies LLC, Research Division

Well, good morning, everyone, and welcome to another great session here on the last day of our 2021 Jefferies Virtual Global Health Care Conference.

We've had a great week, obviously, this week. And one of the teams, I'm obviously looking forward to meeting with here today is FibroGen. We have the CEO, Enrique Conterno, here with us. And obviously, a lot going on at the company and obviously, gearing up for some important decisions and important events this year.

I would just love to start off, Enrique. Maybe you could give some opening comments about where FibroGen stands today with roxa, obviously, both the U.S. and the European developments kind of going on simultaneously. And that would be great as you prepare, obviously, for an AdCom and a whole lot of different scenarios. So that would be great, to turn it over to you.

Enrique A. Conterno

CEO & Director

Thank you, Michael, and great to be here, be able to chat with you once again.

We continue to be enthusiastic and excited about the opportunity of roxadustat to be able to reach patients around the world. Let me cover briefly how I see the different regulatory discussions and then I'll move into also China and the -- basically we're commercializing, which I know is of interest as well.

When it comes to the U.S., we do have an AdCom coming very soon, July 15. We -- maybe my level of enthusiasm is because of -- also of our preparation. We feel very good about our preparation and how diligent we've been, and we look forward to basically having a really good discussion about the benefit/risk profile of roxadustat, which is really the intent of all of these AdComs.

I expect this will be done for each one of the indications that we're pursuing in DD and NDD. Keep in mind, I think what -- and I think it's important that I highlight that roxadustat has shown comparability when it comes to both placebo in NDD and relative to EPO in DD.

And while we are -- when we look at the hazard ratio of -- in incident dialysis, well, it is not below -- while the upper bound is not below 1, the hazard ratio, the estimate is still below 1, and it looks very, very positive. We can comment more way, this is important. And I think it's a reason for us for our success in China as well.

Clearly, Europe is also coming quickly. Astellas is the sponsor for that application. And at this point in time, they've guided towards an approval, including -- they basically have provided a forecast for roxadustat for the fiscal year 2021 across both Japan and Europe, about \$80 million. And it is pretty clear that they're also been enthusiastic about the ability for us to be able to reach patients with this important product.

Now beyond approval, I think it's important that what can we learn from our success in China and Japan, but let me comment a bit more about China because we -- the last quarter, we recorded net sales to distributors of \$43.5 million.

I think it's fair to say this is -- this has been a very successful launch. We feel very good about where we are, including -- basically, at the end of the day, is how health care professionals and patients are basically responding to roxadustat, which is they are getting great feedback, great results in real life, and as a result of that, they have continued to adopt the product as a main staple as part of their practices. We continue to see those trends in the same direction that we've seen in over the last few quarters, which has been a constant of sequential growth. And we feel very good about where we are in China. And as I mentioned before, I think we have guided in terms of China in the area of anemia of CKD as having big sales, north of \$500 million, not \$500 million, but north of \$500 million, we clearly continue to

see this. AdCom is coming quickly. I know there's a lot of high level of interest in that. And I think you will see us very well prepared to address all the questions from the panel.

Question and Answer

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. That was good. And I think there are 3 unique areas of value: U.S., Europe, China and each is kind of a different moving part. Let's take those chronologically. I mean, I guess, in the United States, which, let's be frank, is perhaps, in my opinion, the largest opportunity.

There is consternation amongst Wall Street because there wasn't -- there was not expected to be an AdCom. Now there's an AdCom. You're preparing for that AdCom. What do you think drove the change in the thinking for an AdCom such that it's even in a different AdCom division than the actual filing? Like how do we tie that together because does that say something? What does that imply? Have you had discussions with that regulatory group who's doing the AdCom?

Enrique A. Conterno

CEO & Director

Yes. The division that is reviewing the file continues to be the same. This is the hematology division. I -- as you know, I think in the FDA, you have the divisions and then you have the office. The office is the one that calls for the AdCom. And the AdCom that is related to this office is the renal and cardio AdCom.

So I'm not sure -- honestly, I'm not sure there's a change there. It just -- if there were to be an AdCom, that's how things would have proceeded. So this is not a matter of having an extension and having an AdCom that comes very, very late. So clearly, I think when it comes to any products that will be looked at in this area, in DD and NDD, purely cardiovascular safety is a key topic, and it's of key importance. And we expect that we're going to have all the appropriate expertise to ensure that the benefit/risk profile of the product is discussed extensively and that's what we are ensuring that we're prepared, so we can answer any questions.

Michael Jonathan Yee

Jefferies LLC, Research Division

Have you been engaged with that review group who is in that AdCom and doing that? Like there must be people there, have they had meetings with you? Do you have the draft book? Do you kind of know what's going on there?

Enrique A. Conterno

CEO & Director

Yes. There's really no contact between a sponsor and AdCom members. In fact, I think they look for AdCom members that have -- that can clear conflict of interest. So -- and no, we have not received the Ad book.

We are working closely with the FDA when it comes to analysis and so forth. And I think it is important that walking into the AdCom to be as aligned with the FDA as possible. And how do we interpret any type of different analysis and so forth. We do submit a briefing book, basically, 30 days before the date of the AdCom to the FDA. And I -- at this point in time, I think we continue to prepare, and we look forward to having that day.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. In the scenarios from that AdCom, we could have a really positive vote, we could have a mixed vote. We can have a negative vote. We could have positive and negative votes by indication because you did say you think that the benefit/risk will be taken independently for non-dialysis and dialysis. And presumably, you think the risk/benefit is great for both.

Do you believe that those -- that the FDA sees there to be a difference in benefit/risk there one versus the other? Because, honestly, non-dialysis is a different patient population than dialysis. And it was running against a placebo whereas everyone -- these other sponsors claim that they want it against Aranesp. So maybe just make a comment about the benefit/risk in non-dialysis versus dialysis because some people believe there might be a split label here.

Enrique A. Conterno

CEO & Director

Yes, that's not our view. We believe that we will get a broad indication, so covering both DD and NDD. I think it's important that we maybe take a step back and talk about some of the benefits of treating anemia. Probably the one that is most pressing and one that we've seen as part of our extensive clinical trials, is basically that roxadustat was able to reduce the risk of transfusions.

Clearly, given that we were comparing to placebo, that benefit was very significant in our trials in NDD. As you know, when it comes to patients having transfusion, the more transfusions that they have, it lowers the risk of the potential for transplantation sometime in the future.

So we view, and I think we -- that's -- we view, I think, the benefits of the product has been very significant. Something that is probably that we have come to understand a lot better in China as well, which is something that we don't talk maybe enough about.

But clearly, there is a -- having a novel product is something that is pretty important. Keep in mind that in NDD, which is the population that you were asking a bit about patients, about 90% of the patients actually have to go to a physician office to get their ESA treatment.

So having an oral alternative, I think is going to be quite important for those patients to truly have access to treatments that are accessible truly and convenient. In addition, of course, to all the clinical benefit that we've mentioned, including that roxadustat is just a more physiological way to be able to treat anemia, right?

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes, yes. Okay. And then as regards, let's say, we do -- so we do -- I mean get approval for both, do you believe that the FDA sees cardiovascular risk differently as well in non-dialysis than dialysis? Because I think you've spoken before about the fact that, hey, if you're treating against a placebo, how can one say that there's greater cardiovascular risk, then again, some people believe it's a class effect.

They just stick all "ESAs" there and just slap the same label because the FDA is conservative. Now at this point, it feels like the stock and the valuation of the company doesn't reflect any of that at this point anyways. But that's always an important idea. If you do get approved because you're confident in approval that the black box would be construed differently. How do you feel about that?

Enrique A. Conterno

CEO & Director

Yes. It's -- clearly, we don't -- I don't want to speculate on what the label may look like even we need to see the discussion of an AdCom. And quite frankly, I think when it comes to the AdCom, you are going to have panel members there that are going to be providing their views with different experiences and so forth.

And the FDA will, of course, take all of that input into consideration when thinking about both approval and potential labeling. But the data pretty clearly shows in our view that we are comparable to placebo. And I do believe that the FDA makes all efforts when it comes to label to ensure that the label for the respective product is the one that is included as part of that. I think I've been pretty consistent on that, and I think we've seen it across many different classes.

Michael Jonathan Yee

Jefferies LLC, Research Division

Can I ask a question, this is a nuance, but it's actually come up and that relates to this, which is we talk about class labeling. And is the class defined as ESAs, such that it is erythropoietin-stimulating agents? Or is it the idea that any mechanism that stimulates erythropoiesis, ESAs as erythropoiesis-stimulating process, not stimulate erythropoietin, do you -- can I just ask question -- because we actually did some work on this and the term ESAs or the class of ESAs -- because there's only been one mechanism, so it's almost like they're interchangeable.

Do you think that the FDA may view the concept that the mechanism being different is actually a different process, and that is not stimulating erythropoietin? Again, sort of that nuance because it's actually interesting because how would you argue that the mechanism is quite different?

Enrique A. Conterno

CEO & Director

Well, the mechanism, I think it is quite different. And I think I don't want to speak for the FDA, but clearly, maybe if they didn't think about that differently, maybe we wouldn't have the AdCom, right? So it is a different mechanism. Now -- and we do see different things, right, with the HIF versus an ESA. And we are very excited about providing that alternative to patients.

Keep in mind one thing, Michael, I think when we think about dialysis dependent, right -- because let's not go just to the mechanism, and let's go to the actual -- what we actually see, right? It is pretty clear to me that today, there are a number of patients on dialysis that basically are having a tough time managing their anemia. Part of this is because they are hypo-responders. So -- and this is very well documented. You have to continue to increase the ESA dose. Dose increases have their own element of risk.

So in a certain way, having this new medicine would basically provide an opportunity for many of those patients that actually need an alternative to be able to manage their anemia.

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes.

Enrique A. Conterno

CEO & Director

I think that's pretty clear. And we saw that reflected in our data, right, in particular, for people that had high elevated CRP.

Michael Jonathan Yee

Jefferies LLC, Research Division

I guess I would just argue that if the idea of erythropoietin, which is a recombinant protein, that is what EPO is. Yes, that protein does stimulate erythropoiesis to make more red blood cells. Your drug, because it gives you system ESAs, you're stimulating erythropoiesis but doing it in a different mechanism.

That's all I wanted to say. We don't know that giving greater erythropoietin protein is driving a different etiology than what your drug is. I just want to say that it's class label.

Enrique A. Conterno

CEO & Director

Yes. I appreciate you saying that. And it's -- once again, we look forward to having the discussion at the AdCom. I think we have very comprehensive data. So we -- it's great to have so much data because it's the opportunity to be able to answer fully questions of the panel.

Michael Jonathan Yee

Jefferies LLC, Research Division

So when you're going to get to a panel, you've submitted or about to submit your briefing document.

Enrique A. Conterno

CEO & Director

Yes, we have not -- but -- submitted the briefing doc -- briefing document gets submitted, I believe, 30 days prior to an AdCom.

Michael Jonathan Yee

Jefferies LLC, Research Division

Then the FDA will give you a briefing document weeks before.

Enrique A. Conterno

CEO & Director

That's right. They will -- I mean, the way things work or they should work is that we are -- that we need to work collaboratively with the FDA to ensure that the panel can have the best discussion.

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes. Should that happens and then whatever happens with the vote, do you expect that a PDUFA obviously, which never got renewed, do we just go in sort of a black hole and you'll just say, hey, look, we're in discussion with the FDA and there's no defined deadline, then we can move on from the U.S. Is that fair?

Enrique A. Conterno

CEO & Director

Yes. I wouldn't describe it as a black hole, but yes, we don't -- the PDUFA date can only be extended once, which it was. So therefore, at this point in time, there's no other -- there's not a new PDUFA date. I think, fortunately, we were quite advanced with the FDA on labeling discussions in December. So I am hopeful that post the AdCom, the FDA will be able to take action.

Michael Jonathan Yee

Jefferies LLC, Research Division

Yes. Good. Thank you for bringing that point, I mean the point that you were as of December in labeling discussions and, quite frankly, AstraZeneca, your partner put in the press release that they look forward to continued discussions.

And I think they did actually use in the press release the word label. I think that's actually -- it was not like they got stuck halfway through whether this thing is proved or not, it was actually trying to figure out the label.

Now whether that's carving out a label, labeling in a certain way, black box, I just want to be clear, let's reemphasize that you were actually talking about labeling discussions, and you were down to that level.

Enrique A. Conterno

CEO & Director

Yes. So I think we were -- clearly, now we do have the AdCom. So you were asking timing after that. And we're hopeful that things could proceed that the FDA could take action quickly because of those advances.

Michael Jonathan Yee

Jefferies LLC, Research Division

Because you were fairly deep into everything in.

Okay. And then in Europe, really quick, what you've done in Europe. Look, Astellas has put out financial quidance. Can you speak to the idea of that process, meaning there's a CHMP recommendation.

I know there is member states and I think select representatives that actually lead that. But in general, do you have insight into that at all other than just what Astellas says, your insight and feel like that's going in a different way, and you feel very good about that?

Enrique A. Conterno

CEO & Director

Yes. We continue to feel good about our -- the review process in Europe. Clearly, the next step would be an opinion. CGMP will provide an opinion.

And that's coming quickly. And as you know, from that opinion then -- assuming a positive opinion, then an approval would come a couple of months after that.

Michael Jonathan Yee

Jefferies LLC, Research Division

How are we thinking about appealing? Is that -- now they meet once a month. Do I need to check my Friday of June and July and August, and it could come on any one of those?

Enrique A. Conterno

CEO & Director

Yes. We're not providing more comment, that's really a question for Astellas, but we've guided towards an approval in midyear, so I think you can do the math, right?

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. Well, I want to get really nuance, I guess, is approval means the actual label or approval means the recommendation because the approval comes 2 months after the recommendation?

Enrique A. Conterno

CEO & Director

Yes. Approval is approval and opinion is an opinion.

Michael Jonathan Yee

Jefferies LLC, Research Division

Well, I better check my June calendars, my associate team is on that right now.

That's good. That's good. And again, we cover Astellas out of Asia, and they're saying Astellas is quite positive, too. So that would be a surprise upside, certainly, if we can have that. Good.

What about China? I'd love to spend a couple of minutes there because interestingly, we have the development of the approval, the launch has gone well. Maybe just talk to what's going on there and how that seems to be quite independent of everything going in U.S. and in Europe? Like did you tell them also about the change in the statistics on incident dialysis. Is there label change at all?

I have not read the Chinese label, and I got to put that through Google Translate. I don't read Chinese. But what is that? Do they have a superiority label for things? Or what are they saying at all?

Enrique A. Conterno

CEO & Director

No. If you recall, I think the China submission was based on China data, China trials.

Michael Jonathan Yee

Jefferies LLC, Research Division

This, efficacy. Right.

Enrique A. Conterno

CEO & Director

Yes. And so that happened prior to us submitting in the U.S. and so forth. So these data from the pivotal trial were utilized in the U.S. was not utilized for that approval.

Michael Jonathan Yee

Jefferies LLC, Research Division

Right.

Enrique A. Conterno

CEO & Director

Clearly, China is going extremely well. We've highlighted the significant listing progress that we made over the quarters. We are now roughly about 75% of listing, so 75% in terms of the amount of coverage of the anemia of CKD China market. That's very impressive. And we see basically increased adoption. We've seen sequential growth every single quarter, basically, the quarter number 5 after we got reimbursement with \$43.5 million worth of net sales to distributors.

We feel good in terms of the feedback that we -- and I have been emphasizing this, the feedback that we are receiving from not just key opinion leaders, but general health care providers, professionals, it is pretty clear that they see significant value when it comes to roxadustat and the ease of use, and we see that basically reflected in the numbers.

Maybe an update I can provide to you, it's basically reported, but China just issued new guidelines, anemia of CKD guidelines, stand-alone guidelines. So that's pretty important. Sometimes you have anemia guidelines. Sometimes you have international guidelines, but these are the first stand-alone guidelines in China for anemia of CKD. So -- and roxadustat is very well positioned.

So we are excited about that. We just basically got done. I believe it was maybe June 1 or late May, but this is a very recent development.

Michael Jonathan Yee

Jefferies LLC, Research Division

What -- so it's like treatment guidelines. What does that say in a nutshell?

Enrique A. Conterno

CEO & Director

Well, in a nutshell, it basically provides the framework for treating anemia, first of all, which is very key. And the importance of treating anemia and the goals of treating anemia that is important because one of the significant opportunity that we basically see, basically the growth of this market. And let me comment just a little bit more about that in just a second.

But so you basically look at targets and then the alternatives, right, that should be utilized in both DD and NDD and being formally including this in guidelines because treatment by roxa is still new therapy in China, right?

We are talking about 5 months post reimbursement -- or 5 quarters post reimbursement. So the opportunity for increased adoption is significant. Something that we've noted, Michael, and -- but I think it's -- we expected some of these dynamics, but the way that they're presenting, I think, it's very interesting when we look at the overall growth of the anemia treatments in China. Keep in mind that post roxadustat being introduced, which, by the way, now roxa is basically the #1 brand for anemia of CKD in China. But post it being launched in China, we've seen actually the growth of ESAs accelerate.

Michael Jonathan Yee

Jefferies LLC, Research Division

You're growing the market, you're growing the market, and these treatment guidelines are going to help that.

Enrique A. Conterno

CEO & Director

Correct. And so I am so encouraged by this because I think it bodes very well for the overall expansion of the market and in particular, when it comes to NDD. And to me, I think I view the adoption by physicians that we basically see in China as a great signal what we could see in some other markets around the world.

Michael Jonathan Yee

Jefferies LLC, Research Division

Let me ask one final question because I know we're 1 minute over. But with the change of the statistics around some of the analysis, I know that ASN has some comments on their publication, if you go to that. And I know that you guys are working through those changes. You've actually been communicating with FDA and doctors, I guess. But it's not a true -- so there's not really -- this is investigational. But are you working to get that publication fixed at all? And maybe just make a comment on that.

Enrique A. Conterno

CEO & Director

We do. I think clearly, I think we want to make sure that the -- what's out there when it comes to incident dialysis is basically -- and MACE, basically, reflects the data that we've talked about when it comes to the prespecified certification factor. So we are in the process of working through that. And at this point in time, I think we made quite a bit of progress.

Michael Jonathan Yee

Jefferies LLC, Research Division

Okay. Well, look, you guys were in final negotiations, and then we have this AdCom show, it is far down the review path. You guys -- obviously, it sounds like we just want to get some clarifications on this done. So hopefully, that doesn't turn everything so far upside down. You are already in label discussions, and we'll hear that.

We've got the briefing documents set up, and we'll hear about that over the next month. We'll see you on the July 15 review in Europe, which I just figured out too, could happen at any point. Good. Thank you very much.

Enrique A. Conterno

CEO & Director

Very good. Thank you very much, Michael.

Michael Jonathan Yee

Jefferies LLC, Research Division

All right.

Enrique A. Conterno

CEO & Director

Great seeing you.

Michael Jonathan Yee

Jefferies LLC, Research Division

Of course. Thank you.

Enrique A. Conterno

CEO & Director Bye-bye.

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EXHIBIT UU

S&P GlobalMarket Intelligence

FibroGen, Inc. NasdaqGS:FGEN Company Conference Presentation

Thursday, June 10, 2021 8:00 PM GMT

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EXECUTIVES

Enrique A. Conterno *CEO & Director*

ANALYSTS

Kyuwon Choi Goldman Sachs Group, Inc., Research Division

Presentation

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Okay. Welcome back, everyone, and thank you for joining us on Day 3 of the 42nd Annual Goldman Sachs Global Healthcare Conference. I'm Paul Choi, and I cover the mid-cap biotechnology sector here at the firm. And our next session will be with FibroGen.

Joining us from management is CEO, Enrique Conterno. What we'll do as in prior sessions is we'll turn it over to Enrique for some opening commentary, and then we'll go into Q&A. [Operator Instructions]

But otherwise, with that, we'll turn it over to Enrique.

Enrique A. Conterno

CEO & Director

Thank you, Paul, and thank you for the invitation. A few comments on FibroGen. We are, of course, excited about the -- having the outcome with the -- here in the U.S., and the preparations are going well. The outcome is July 15. Also waiting for the regulatory decision in Europe. That's another important milestone for us.

And of course, I think, continue to be very bullish about our performance in China with roxadustat. So all eyes in roxa, U.S., Europe, China. But we should not forget pamrevlumab, which is our monoclonal antibody, anti-CTGF, basically pursuing 3 indications in idiopathic pulmonary fibrosis, locally advanced unresectable pancreatic cancer and Duchenne muscular dystrophy. And those trials are enrolling well. We have -- we expect readouts for 2 of those indications in the second half of next year.

And finally, something we don't often talk about, but it's our belief that we can bring new product with significant clinical value into the clinic. So we've been working both internally and also looking externally to basically strengthen our overall early pipeline. So I look forward to your questions, Paul.

Question and Answer

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Okay. Thanks, Enrique, and thanks for joining us. Maybe starting with roxadustat in China, we can start with the commercial piece. And you and your partner provided a recent commercial update on the earnings call. But can you maybe talk a little bit about how it's progressed since your last update? What is market uptake like? And I had a follow-up on that as well.

Enrique A. Conterno

CEO & Director

Yes. It's very exciting to see the performance of roxadustat in China. We commercialized the product with AstraZeneca. We have a 50-50 profit share in China, just to remind everyone. And I think what's exciting is basically looking at the adoption of the product, adoption-driven because we are -- we've been now listed in north of 70% of hospitals that comprise -- sorry, hospitals that comprise 70% of the overall anemia CKD opportunity in China. And then, basically, adoption within those hospitals.

Our revenue -- sorry, our net sales to distributors in Q1 of this year was \$43.5 million. That's basically quarter 5 after updating reimbursement in China. So very significant uptick for the product. I think one thing probably that is worthwhile highlighting is that when we look at the market dynamics in China, what we basically see is now roxadustat becoming the #1 brand in terms of value in China for anemia of CKD, but importantly, when we look at the rest of the market, ESAs, when we look at the ESAs, we've actually have seen that ESAs growth has actually accelerated since the launch of roxadustat.

So all of -- I think that speaks extremely well for the overall health of the overall market. The growth that we're seeing -- and I expect that growth has significant led for not just months, but for quarters and years to come. So very excited about what we basically see there.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Could you maybe dive a little more into where you're seeing the growth and adoption in China so far? Are you seeing it primarily in the dialysis setting, incident dialysis and maybe -- or NDD populations? Just help us understand how the practitioners and clinicians and dialysis centers there are taking a look at adopting roxa?

Enrique A. Conterno

CEO & Director

We do. I think the -- let me first try to break that down for you. Around 65% of the volume we see basically roxadustat being utilized through dialysis centers or dialysis settings. The rest basically is non-dialysis-dependent settings. What is important to highlight is maybe that the use of roxadustat is pretty broad. And if there was a surprise that we've had since we launched in China was basically the uptake in NDD. We know that the potential in NDD long-term is very high. So we expect good growth for many years as we build that market. But what we've seen is basically faster uptick than maybe we were expecting in that particular setting.

The areas where we see the product being utilized should not be a surprise. We see basically patients, incident dialysis patients, patients that are hyporesponders to ESAs and in -- most of the growth is, when we look at roxa, I mentioned where our growth is coming, but we look at the overall market, I -- we don't have very definitive data, this acceleration that we see in the overall market, it is because we are seeing basically NDD basically taking off. So I think that's very exciting. And we view that as a very significant long-term opportunity for us.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Maybe one more on the commercial piece here before switching to the regulatory side, which is you talked about the unexpected growth in NDD. But as you take a look -- and you think about the opportunity and how you think about the revenue composition over the longer term. How do you think about that NDD being a portion of your longer-term revenue mix in China versus the dialysis setting?

Enrique A. Conterno

CEO & Director

Yes. What I -- I think what we've said, not just for China, but in general, is that we expect that dialysis would be faster uptick, but we believe that the NDD opportunities significantly larger, meaningfully larger than DD. So we expect that opportunity to be larger over time. Maybe something to -- worth highlighting, Paul, is that China has recently issued guidelines, stand-alone guidelines for anemia of CKD.

And roxadustat is front and center on some of those guidelines. So we're pleased with how roxadustat is recommended as part of those new guidelines. But I think what that's telling you is also that is exciting, that's going to basically -- is a reaffirmation of better the decision that health care professionals are making in China to utilize roxadustat more and more often.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Maybe we can pivot now to the U.S. regulatory piece. And I guess, question one is, have you had any subsequent interactions or even at an informal level with the FDA since your last update to the street with your quarterly results? And then I had a couple of follow-up questions.

Enrique A. Conterno

CEO & Director

Yes. Clearly, we are working towards the outcome, and that involves quite a bit of preparation. I believe those preparations are going very well. And as part of that, we have exchanges with the FDA, and it is, I think, in the interest of everyone to ensure that the that we can go into that -- into those meeting extremely well prepared so that the AdCom panel can have the most productive discussion possible in that setting. And yes, we've had productive and good discussion with the FDA in preparation for that.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Has the agency any -- offered any sort of commentary that would strike you as sort of different from the way you guys are thinking about it in any sort of meaningful way? And have they provided any suggestions that maybe -- or commentary that -- versus your thinking on how to approach the AdCom that you would sort of message to the street as being potentially novel or incremental?

Enrique A. Conterno

CEO & Director

No. My -- first, I think we don't comment on the regulatory interactions with the FDA. But clearly, I think the discussions are intended to, yes, look at how -- try to understand how the FDA and how we are interpreting all of the data, what are -- is in our interest to understand where the focus will be. As you know, the FDA will have a briefing book. We are preparing one as well for -- to submit to the FDA, and that's -- so all of that, I think, is going to be important, I think, for the AdCom.

But one thing that is -- when it comes to any type of AdCom, it's sometimes difficult to predict the exact topics of discussion with the AdCom because we are bringing AdCom committee member that they have a lot of expertise, and they're bringing that external perspective, external to the FDA.

So the interest is to make sure that the briefing books are as clear as possible, and that the discussion can be as productive as possible. But from our perspective, we need to be very well prepared and broadly prepared so that we can address any type of questions that they may come.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. A little while back, you provided an update on the longer-term roxa data that you previously presented at Kidney Week 2019 that resulted in some changes in some of the cardiovascular hazard ratios and ranges for roxadustat across the various populations you've studied. And so I guess, as you look at that update as you -- and as the company and regulators have digested that updated data, can you maybe update us on your thinking of what the safety signal is, what is the messaging there? And then as a follow-up to that, has the agency expressed any particular view on what -- how to think about the statistics?

Enrique A. Conterno

CEO & Director

Yes. I think what the data -- what the data shows is -- what the analogy shows is basically the roxadustat is comparable to ESAs to EPO in the DD setting and comparable to placebo in the NDD setting. And I think that's what we basically can say based on how we conducted those studies.

Clearly, when it comes to the AdCom, we have to be -- we're very well prepared when it comes to MACE, but we've got to be prepared for any topic that may come and ensure that we're providing all of the appropriate background when it comes to anemia of CKD in order to have the full discussion.

We -- you may recall that we shared that we had communicated to the FDA when we made some of those changes, the data had both sets of analysis have been submitted to the FDA that were part of the NDA. So that discussion was a productive one. We shared at that time. And at this point in time, I think we feel good going into the outcome.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Okay. Great. Maybe in terms of your preparations themselves, can you maybe talk to us about what are you doing? Are you doing mock AdComs? What sort of practice runs or preparations are you doing here? And then I had a follow-up to that.

Enrique A. Conterno

CEO & Director

Yes. I think the preparation for an AdCom, I think, is -- tends to be pretty rigorous. I would almost describe it as a bit of a science, but there's some art to it as well. And I think you want to make sure that you are creating the situation that is as comparable to the outcome as possible. So yes, you do a number of mock rehearsals, if you wish, they have a formal feedback, formal briefing books, and you get advice and in some cases, criticism, the intent is to make sure that we can learn from each one of those rehearsals to be prepared as possible for questions that may come. What was helpful for -- towards the understanding, and at the end, making sure that the discussion once again can be as productive as possible. I think it's in everyone's interest.

Kvuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. You brought up something interesting earlier, which is that you said you have to prepare for any type of question. And so I guess, as you and your team and outside consultants, think about what the AdCom could look like. What do you think about key topics and potential vote questions could look like as the AdCom approaches here on July 15?

Enrique A. Conterno

CEO & Director

Yes. Clear, I think it's difficult because I think, as you know, I think those questions would depend on the briefing books, and also on the questions that the FDA is asking the outcome to basically brought on at the end of the day. But I think the expectation, as is in every outcome is that the FDA will be seeking

feedback on the benefit risk profile of the product. And I expect this is going to be done for each one of the indications, DD and NDD.

We do have to -- when I say we have to prepare broadly, I think it's important because we are -- we might be a little bit closer to the product, and we have to -- while there are going to be briefing books and so forth, those need to be helpful so that the AdCom committee members can have all the background, not just on the product, but on anemia of CKD and ensuring that there is a full picture and a full understanding of that, so that the appropriate assessments and the appropriate discussions can happen.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Maybe taking a bigger picture view, how do you and the company sort of think about the agency's stance on the headset as a class. Especially given the updates on your side as well as the recent NDA acceptance of Akebia's vadadustat not too long ago. And so what does that, from your perspective, say to you about the agency's stance on the class?

Enrique A. Conterno

CEO & Director

I mean, it's -- I'm not sure what I would make of it. I think the FDA tends to be very focused on the data of the sponsor. So there are a number of examples where products from the same class have received very different labels based on their own data. And this is particularly important when the data is -- tends to have the number of patients, as you basically see in cardiovascular study.

So when it comes to cardiovascular studies, you basically see the FDA labeling for each particular product to basically be reflective of what those specific trials demonstrate as opposed to thinking about all products are the same. It is not that only the first product in the class gets asked to conduct CV studies, all of them ask and then -- so I've seen the -- the experience that I have is that the FDA tends to be quite focused on the specific data. And I think that's what will carry the day for us, which is, I believe the FDA will focus on the overall roxa data in each DD and NDD as they make their assessment and decision here.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. You also earlier brought up an important point, which is that, obviously, roxa has been developed and filed for European filing and the MAA filing is under review here with a potential decision coming up here during the summer. So how do you think you and your partner -- think about that opportunity? And sort of what are the next steps there for a potential commercial launch in the European market?

Enrique A. Conterno

CEO & Director

Yes. Clearly, the -- our partner when it comes to Europe and Japan is Astellas. So they are the sponsor in Europe. I -- the discussions with the regulator are I would describe them as proceeding well. But it is probably a better question for Astellas than for us. What I can share is, I think, maybe just highlight what Astellas has communicated. They recently provided guidance for roxadustat when it comes to fiscal year 2021. They shared that they expected revenues -- net revenues from roxadustat to be and I'm translating from yen here, but about \$80 million.

And they also provided recently as part of their strategic overview, long-term projections for roxadustat for their territories, Astellas' territories. So this includes Japan, Europe and a few other smaller territories. But the projection that they provided, if I recall correctly, was JPY 50 billion to JPY 100 billion, which you would translate -- I don't know what the exchange rate is today, but at the time I translated that, it was about peak sales somewhere between \$450 million and \$900 million for those geographies.

So we are excited about the opportunity to have these products reach patients in Europe, but really across the world. And you're right, I think that we are expecting, I think, the opinion, I think, any time now.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. And could you maybe just sort of broadly remind us of the economics with your partner there, Astellas in those territories?

Enrique A. Conterno

CEO & Director

Yes. We basically have a royalty we share for both of our partners in the low 20% range.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Okay. Great.

Enrique A. Conterno

CEO & Director

So we are fully reimbursed on all development and commercial costs outside of China. I think that's important to mention. In China, where we have a 50-50 profit share, but outside of China, we basically would receive a royalty.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Turning to the commercial side here in the U.S. Can you maybe help us understand what is sort of the state of the union with regard to dialysis here in the market in the U.S. as you think about a potential roxadustat launch over the near-term in the U.S. and just kind of what is the impact from COVID as you're launching potentially in the near term?

Enrique A. Conterno

CEO & Director

Yes. Clearly, honestly, we are extremely encouraged from our learnings in China and how much -- how the fast adoption that we've seen for the product in China. Clearly, the dynamics in the U.S. are different from a payer perspective, and I'll discuss those, but I believe that physician adoption will be basically similar to what we basically see in China with faster adoption maybe in the dialysis setting. And in NDD adoption over time, but once again, the opportunity in NDD is significantly larger over time.

Clearly, when it comes to DD, the framework for reimbursement is TDAPA. This is a payment adjustment or an additional payment that would be done that the dialysis organization will receive that would be outside of the dialysis bundle. TDAPA is designed to basically foster innovation. And it had last for a period of 2 years. And our preparation is to ensure that once we receive approval in the U.S. that we can submit for TDAPA eligibility right away.

And TDAPA eligibility becomes effective. The first day of a quarter, so that's going to be key, I believe. And that's really the true catalyst for use, I think, in the dialysis setting. When it comes to NDD, I think the reimbursement is a bit different. It's a matter -- the Medicare opportunity is slightly north of 50%. Commercial, maybe about 30%, and then Medicaid, the rest.

And in order to ensure that the product can reach patients, we will need to be included in formularies. And clearly, for the NDD setting, that would be extremely important. And I think there are a number of benefits that I think that we can highlight for payers. But once we have that coverage, if you wish, across the different settings, I expect that the decision adoption will be very fast.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. I do want to talk about the other parts of the pipeline, but maybe just one more on the commercial piece, which is that clinicians are typically not used to treating patients with ESAs in the NDD setting, it's

kind of a novelty there. So how do you think about receptivity and how do you think about driving changes in physician behavior there?

Enrique A. Conterno

CEO & Director

Yes. Clearly, it's 2 things that really matter initially is going to be basically, okay, the label that we have, what is the label saying? But then also the experience -- the initial experience the physicians will have with the product. There are a number of clinical benefits, I think, which I think we've shared before, but I believe, for example, in the dialysis setting, we are going to be utilized in incident dialysis, our patients are starting dialysis, I believe that roxadustat can be the product of choice there and also when it comes to patients that are hyporesponders to ESA.

And in NDD, I think for the most part, most patients are not treated, but we have to recognize that outside of all the clinical benefits, I think there are significant limitation for the use of ESAs in that setting, including that patients have to go to physicians' offices to have the product administered. So we view, I think, roxadustat offering significantly more convenience as well in addition to some of the clinical space.

That -- I mentioned that because I think I failed to mention that in the past and what I -- what we basically see in China is that, that might be a pretty important engine for growth and to increase treatment rates, which at the end, I think it's going to be key, I think, when we look at the NDD segment.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Okay. Great. Let's spend a little bit of time shifting to pamrevlumab, and you focused on 3 development opportunities and maybe we can start with IPF here. Can you maybe just help us understand what's going on and what sort of the enrollment progress with your 2 ZEPHYRUS studies coming out of COVID here and just sort of perhaps provide an enrollment update for us?

Enrique A. Conterno

CEO & Director

Yes. What we basically have seen is as the COVID situation has improved, and particularly, in the U.S. first, we've seen significant improvements in enrollment across all of our trials. But probably most meaningful when it comes to our ZEPHYRUS IPF trial.

I think it's important to remind everyone that when it comes to IPF, the data that we produced in that pamrevlumab showed as part of our Phase II is very meaningful. We view that data as basically showing the meaningful effect size, highest -- largest effect size of any product in IPF, whether they are in the market or in development.

So if we were to replicate those type of results, I think that will be incredibly important for patients. We have not provided guidance when it comes to when would we expect a reader for IPF, but we expect to provide guidance very soon.

We are seeing improvements in enrollment, in particular, when it comes to U.S. and probably driven by, as I mentioned, the overall COVID situation improving in the U.S., but also because there was a failure of a competing product that has made a number of sites and also patients eligible now for pam. So we are excited about basically what we're seeing.

Outside of IPF, we have 2 additional indications that we're pursuing. And both of those are expected to read out in the second half of next year. And they are -- we are seeing LELANTOS-1 enrolling well. This is the trial for DMD. And then we're seeing LAPIS, the trial we are conducting for locally advanced and resectable pancreatic cancer, also enrolling very well. So we are excited about having those readouts coming in the second half of next year.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Specifically, perhaps with regard to the pancreatic trial, can you maybe just remind us what is considered a successful result with regard to the endpoint and respectability? And just as you mentioned, timing would be second half of next year, potentially. And how is that data contextualized in the setting of the current parent treatment paradigm?

Enrique A. Conterno

CEO & Director

Yes. Clearly, I think they are very, as you know, very limited options when it comes to unresectable pancreatic cancer. So having a positive trial in -- for that population will be huge. It's a huge unmet need. It's -- when we -- you're correct, when we're thinking about the readout that we will have is a readout based on certain number of resection events.

And clearly, I think we need to see a separation, important separation there. The -- based on that readout, we expect to, assuming it's positive, we expect to ask for an accelerated approval and have the discussion with the FDA.

Of course, they will be looking also at the overall trend when it comes to overall survival and so forth. But clearly, if there is an important difference when it comes to resection, I think we're going to feel highly confident about the overall benefit. So that's key. I think when it comes to overall survival, I think we will have to wait longer for that to finally read out.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Okay. Great. That makes sense. That will take a little longer. Maybe just turning back to IPF for a moment. And you did highlight a competitive failure, but there is still some competitive intensity in the space as well as establish incumbent drugs such as Esbriet. And so I guess, how do you think about the commercial opportunity there? The drugs that are approved are sort of growing at a multibillion-dollar rate here.

And so I guess, is this an opportunity to grow the pie collectively? Or do you maybe think about it more as a share gain sort of a potential market for pamrevlumab here?

Enrique A. Conterno

CEO & Director

Yes. Keep in mind that the needs in IPF are still very significant. And of course, I think we'll have to rely on the data. But assuming that the data, we can replicate the data from our Phase II trial. I believe that pamrevlumab will be used in a very meaningful way as an option to treat patients on -- with IPF.

You keep in mind that the current therapies sometimes are not well tolerated. I estimate that maybe about half of the patients, in some cases, are -- don't tolerate those therapy well and need to look for some other options as well. I think what's important about pam and I think what we showed, I think, in the Phase II trial is not just the clinical efficacy that we typically look at. But also, the reason to believe, because, as you know, the first time that really a product has shown from an imaging perspective, basically, I think the improvement when it comes to fibrosis, right?

So that to me, I think, is very significant. And clearly, I think it could be a huge benefit. We need to wait for those Phase III trials to read out. But it is -- I have a high level of conviction when it comes to pamrevlumab in IPF and the commercial opportunity, as you just mentioned, I think it's very significant.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. While obviously, people are focused on development of roxa for CKD, you are also pursuing development of it in other indications and opportunities. Namely, you're in a late-stage trial for evaluating roxa in MDS. Can you maybe, first, provide us an update on how that trial is going? And then sort of secondly, there is a drug approved from Bristol and Acceleron in this area of anemia for MDS, and just how you think your data stacks up versus REBLOZYL here?

Enrique A. Conterno

CEO & Director

Yes. We are -- as you well mentioned, we are pursuing roxadustat also in MDS. Importantly, that we are in a Phase III trial and the readout for that trial is expected in the first half of next year. So that's coming soon. We are just, for a matter of being complete. We're also, as you know, pursuing chemo-induced anemia and we expect data in the second half of this year for that Phase II trial.

Both opportunities are important to us. Clearly, when it comes to MDS, I think we see, I think, the significant success that luspa is having and we need to wait for a readout, but I think the expectation that we have is that our data is going to be somewhat comparable to the data that luspa has shown. As you know, we're starting our product in a broader population than what luspa initially targeted their trials at.

And when it comes to chemo-induced anemia, we view that, that opportunity as very significant. In fact, the way that we think about it is CKD being the largest opportunity but chemo-induced anemia being maybe an opportunity that could be about 80% of the opportunity that we see when it comes to anemia CKD, but MDS being a smaller opportunity than that.

Clearly, the product that you made reference to is priced differently than an anemia CKD opportunity. I know you've asked me in the past, how would we think about pricing of the product and so forth, that's something that we need to be -- that we need to work through. Of course, it's going to be data dependent. But we need to think about how do we ensure that we can capture the value of the product at the end is delivering. And -- but that sometimes it's difficult to do across indications where the pricing of that is very, very different.

So that's some work for us to continue to do. I think what's -- from a commercial perspective, though, what's in front of us is right now, ensuring that we are ready to launch roxadustat across the world as the regulatory decisions in Europe and U.S. are coming very shortly.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. Thanks for that. We're coming up on time, Enrique, but I did want to go back to something you mentioned earlier, which is you're talking about, at some point in the not-too-distant future, talking to investors about your next wave of development efforts here.

And so could you maybe sort of paint some broad strokes as to where FibroGen might be heading in terms of its next wave of development? You obviously have a lot going on with your current pipeline, but sort of what is the next stage, potentially, of FibroGen look like here?

Enrique A. Conterno

CEO & Director

Yes. Clearly, we need to make sure that first, we leverage the strength of the size that FibroGen has when it comes to both HIF biology and CTGF biology. And it is pretty clear that the HIF biology is quite involved and could have a number of different applications. So we need to make sure that we leverage the opportunities that we have.

Throughout the last 1.5 years, we've done a full assessment of all the programs that we have here at FibroGen, and we've been pretty disciplined to make sure that we are investing on the product that have the most merit. And that we believe have likelihood of truly bringing innovation to patients. So that has happened.

In addition to our internal efforts, we are also looking externally at opportunities. Now we've been pretty diligent. We have not done a transaction as you know, I think we need to have conviction around the science and the clinical opportunity, but also about making sure that we can create value. So we've looked at a number of things, but we've been disciplined in terms of our assessment and so forth, but you should not be surprised if at some point in time, we bring additional assets.

And we are thinking, in particular, in that preclinical space and for signs that we have significant conviction in areas where we think we can move quickly and create a lot of value.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Great. We're just about up on time here, Enrique. So we'll have to end it on that note. Thanks to you and FibroGen for joining us today.

Enrique A. Conterno

CEO & Director

Thank you very much, Paul. Appreciate the invitation.

Kyuwon Choi

Goldman Sachs Group, Inc., Research Division

Yes. Thanks.

Enrique A. Conterno

CEO & Director

Thanks.

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EXHIBIT VV

FDA Briefing Document

Cardiovascular and Renal Drugs Advisory Committee Meeting July 15, 2021 Roxadustat

The committee will discuss the safety and efficacy of the New Drug Application (NDA) 213805 for roxadustat, an oral film-coated tablet submitted by FibroGen, Inc. The proposed indication is for the treatment of anemia due to chronic kidney disease (CKD) in adult patients not on dialysis and on dialysis.

Date Prepared: June 14, 2021

Division of Nonmalignant Hematology

and

Office of Cardiology, Hematology, Endocrinology, and Nephrology

Office of New Drugs

Center for Drug Development & Research

US Food & Drug Administration

Silver Spring, MD 20993

Department of Health & Human Services

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The attached package contains background information prepared by the Food and Drug Administration (FDA) for the panel members of the advisory committee. The FDA background package often contains assessments and/or conclusions and recommendations written by individual FDA reviewers. Such conclusions and recommendations do not necessarily represent the final position of the individual reviewers, nor do they necessarily represent the final position of the Review Division or Office. We have brought roxadustat to this Advisory Committee in order to gain the Committee's insights and opinions, and the background package may not include all issues relevant to the final regulatory recommendation and instead is intended to focus on issues identified by the Agency for discussion by the Advisory Committee. The FDA will not issue a final determination on the issues at hand until input from the Advisory Committee process has been considered and all reviews have been finalized. The final determination may be affected by issues not discussed at the Advisory Committee meeting.

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List of Acronyms

AE adverse event

ALT alanine aminotransferase

ANCOVA analysis of covariance

AST aspartate aminotransferase

BMI body mass index

CI confidence interval

CHF congestive heart failure

CKD chronic kidney disease

eGFR estimated glomerular filtration rate

ESA erythropoiesis-stimulating agent

ESRD end stage renal disease

Hb hemoglobin

HD hemodialysis

HIF hypoxia-inducible factor

HR hazard ratio

LSM least squares mean

MACE major adverse cardiovascular events

MI myocardial infarction

NI non-inferiority

PHI prolyl hydroxylase inhibitor

PD peritoneal dialysis

P-Y patient-year

RBC red blood cell

SAE serious adverse event

TBL total bilirubin

TIW three times weekly

ULN upper limit of normal

US United States

Introduction

This is the FDA briefing material for the July 15, 2021 meeting of the Cardiovascular and Renal Drugs Advisory Committee. The Committee will discuss the data in support of New Drug Application 213805 for roxadustat, to consider its benefits and risks for the applicant's proposed indication: "Roxadustat is indicated for the treatment of anemia due to chronic kidney disease (CKD) in adult patients not on dialysis and on dialysis."

Erythropoiesis stimulating agents (ESAs), such as epoetin alfa and darbepoetin alfa, are typically used in the treatment of the anemia of CKD, and they increase red blood cell (RBC) mass through the same mechanism as endogenous erythropoietin. Roxadustat is an orally administered reversible inhibitor of hypoxia inducible factor (HIF)-prolyl hydroxylases (PH). Inhibition of HIF-PH is thought to increase levels of endogenous erythropoietin, thereby increasing erythropoiesis. By avoiding supra-physiologic plasma levels of exogenous erythropoietin analogues, the applicant hypothesizes that there will be fewer undesirable effects, thus providing a safer alternative to ESAs. The applicant also believes that roxadustat has salutary effects on iron metabolism that will reduce the requirements for iron in these patients. If approved, roxadustat would represent the first drug in this class in the United States (US). Importantly, additional drugs in this class are in late-stage development, and may be submitted to FDA for evaluation.

The NDA includes an extensive database in support of roxadustat's efficacy and safety for both the NDD and DD populations. The development of roxadustat for the two populations proceeded concurrently; therefore, results of the DD studies were not available for the planning of the NDD studies, and vice versa.

For the NDD patient population, three similarly designed, adequate and well-controlled studies support roxadustat's efficacy for the treatment of anemia. These studies, referred to as anemia "correction" studies, enrolled patients with CKD who were anemic at baseline (mean hemoglobin [Hb] ~9 g/dL), and randomized them to roxadustat or placebo. A fourth study was unique—with randomization to roxadustat or darbepoetin alfa—and provides the ability to compare the efficacy and safety of roxadustat to an ESA in this population.

For the DD patient population, there were also three principal studies; these enrolled patients with CKD and incident or stable dialysis. At baseline, the mean Hb was slightly higher than in the studies in the NDD population, about 9.6 g/dL overall. These studies compared roxadustat to epoetin alfa. A unique study, considered separately, was conducted in Europe and permitted the use of two different ESAs (epoetin alfa or darbepoetin alfa). One of the ESAs (Eprex, epoetin alfa) is not licensed in the US and is not considered to be the same as US licensed Procrit/Epogen (epoetin alfa).

As is the case with ESAs, roxadustat is titrated to achieve a target Hb level, and roxadustat's efficacy is not in question. All studies in both the NDD and DD patient populations demonstrated efficacy. The principal issue before the Committee is the drug's safety, and safety with respect to the specific CKD patient populations.

During the development of drugs for the treatment of anemia of CKD, we have generally asked sponsors to demonstrate noninferiority (or superiority) with respect to major adverse cardiovascular events (MACE) for both the dialysis and non-dialysis populations (vs. an active comparator and placebo,

respectively). In this development program, MACE included the following events: all-cause mortality (ACM), non-fatal myocardial infarction (MI), and non-fatal stroke. (The MACE composite here differs slightly from the composite typically used in cardiovascular outcome trials; here all-cause mortality, rather than cardiovascular mortality, was used.) The applicant has provided these MACE assessments, as requested, and they represent an important part of this application.

Placebo-controlled studies in the NDD patient population enrolled subjects with significant anemia, and because anemia was less likely to improve in subjects who received placebo, they were more likely to discontinue from the study. Thus, for the three trials overall, completion rates were 62% and 41% in patients randomized to roxadustat and placebo, respectively. The difference in completion rates confounded a number of the safety analyses; in particular, the MACE results are sensitive to the duration of post-treatment observation.

Beyond MACE, a number of safety issues merit consideration and are described herein.

Roxadustat

As noted above, roxadustat is an orally administered reversible inhibitor of HIF- PH, intended to improve anemia in patients with CKD in both the NDD and DD populations.

Roxadustat is proposed to be available as a film-coated tablet for oral administration containing 20, 50, 70, 100, or 150 mg of roxadustat. The proposed recommended starting dose for patients on dialysis or patients who are not on dialysis and not on an ESA is 70 mg three times per week (TIW) in patients weighing <100 kg and 100 mg TIW in patients weighing ≥100 kg.

Roxadustat is not marketed in the US, but has marketing authorization in the People's Republic of China (December, 2018) and Japan (September, 2019). Both countries approved use first for the treatment of anemia due to CKD for patients on dialysis followed by an approval for patients not on dialysis. Based on the safety data submitted in this NDA, the People's Republic of China has updated the English language version of their label to include safety information for cardiovascular events, vascular access thrombosis, deep vein thrombosis, seizures, and serious infections. The English language version of the Japanese label has a Boxed Warning for serious thromboembolism including cerebral infarction, myocardial infarction (MI), and pulmonary embolism. Additional notable adverse reactions in the Japanese labeling are thromboembolism, including shunt occlusion, and seizures.

Anemia of Chronic Kidney Disease

Anemia is a common complication of CKD that develops early in the course of the disease and worsens as CKD progresses. The overall prevalence of CKD in the US adult population is estimated at 15%, with an estimated 17.2 million having Stages 3-5 CKD. The prevalence of anemia increases as the glomerular filtration rate (GFR) declines [1, 2]. It is estimated that 50% of patients with Stage 4 and 5 CKD not on dialysis and 90% of patients requiring dialysis are anemic. The etiology of anemia of CKD is multifactorial and includes erythropoietin deficiency, impaired ability to absorbiron (iron deficiency), inability to utilize stored iron (chronic disease), blood loss, and shortened RBC survival. Symptoms of anemia include fatigue, reduced exercise tolerance, and dyspnea.

Currently available therapeutic options for anemia of CKD include iron, ESAs, and RBC transfusions. Patients with CKD are routinely monitored for evidence of iron deficiency and treated with iron if deficient. Approximately 8% of patients with Stage 4 and 13% of patients with Stage 5 CKD receive an

ESA. Pre-end-stage renal disease use of an ESA in the adult population by age category ranges from approximately 12% to 17% [3]. Most patients with CKD receiving hemodialysis (HD) require ESAs to correct anemia and reduce the need for RBC transfusion and its attendant risks, including the risks of alloreactivity and rejection after kidney transplantation. In order to place roxadustat into proper context in the armamentarium of therapies for the anemia of CKD, some general background on ESAs is important.

Erythropoiesis Stimulating Agents

Epoetin alfa is a glycoprotein manufactured by recombinant DNA technology that contains the identical amino acid sequence of isolated natural erythropoietin and has the same biological effects as endogenous erythropoietin. ESAs bind to and activate the human erythropoietin receptor and stimulate red blood cell production in the bone marrow. ESA use for these indications has spanned over 30 years.

Currently marketed ESAs include epoetin alfa, darbepoetin alfa, methoxy polyethylene glycol-epoetin beta, and epoetin alfa-epbx. Dosing can vary from three times a week to monthly, depending on the specific agent and setting. All are administered by the intravenous or subcutaneous routes; none can be orally administered.

Table 1: US-Licensed ESAs for the Treatment of Anemia Due to Chronic Kidney Disease (CKD)

Product Names Established (trade)	ApprovalYear		
epoetin alfa (Epogen/Procrit)	1989		
darbepoetin alfa (Aranesp)	2001		
methoxy polyethylene glycol-epoetin beta (Mircera)	2007		
epoetin alfa-epbx (Retacrit)	2018		

Subsequent to the initial approval of an ESA for patients with CKD in 1989, the ESA labeling has undergone significant revisions because of accumulating knowledge from safety surveillance and clinical trials. These labeling revisions have included the addition of a Boxed Warning for increased mortality, serious cardiovascular and thromboembolic events; warnings for hypertension, seizures, and thrombotic events including vascular access thrombosis; and in dosage and administration, a reduction in the recommended "target Hb," and a recommendation to discontinue the ESA in patients in whom Hb does not respond adequately over a 12-week escalation period. Other major adverse reactions of ESAs include thrombosis, hypertension, seizures, and pure red cell aplasia.

ESA use in patients with CKD can confer an increased risk of MACE. Clinical trial data have established that targeting higher rather that lower Hb levels increases the risk of MACE, yet the Hb target that best balances benefits and risks has never been identified for any of the ESAs.

The US Normal Hematocrit Trial [4] was the first in a series of randomized controlled trials (RCTs) designed to test the hypothesis that a higher target hematocrit in subjects receiving hemodialysis (HD)

would result in improved outcomes. A cohort of 1233 patients with end-stage renal disease (ESRD) on HD with symptomatic heart failure or ischemic heart disease was randomized (open-label) to either partial treatment of anemia (hematocrit of $30\pm3\%$) or full correction (hematocrit of $42\pm3\%$). The primary endpoint was death or first non-fatal MI, analyzed by time to event. The trial was terminated at the third interim analysis for futility and potential harm in the full anemia correction group. There were 202 primary endpoint events in the full correction group compared to 164 events in the partial correction group: risk ratio 1.3 (95% confidence interval [CI] 0.9–1.9). Also, 39% of subjects in the full anemia correction group had vascular access clotting vs. 29% in the partial treatment arm (P = 0.001).

The CHOIR study [5] was a randomized, open-label, active-controlled clinical trial in patients with NDD-CKD that aimed to show superiority of full anemia correction by ESA administration in terms of cardiovascular events and death. In this trial, 1,432 patients with CKD and anemia (Hb < 11 g/dL) received epoetin alfa and were randomly assigned to a target Hb of either $13.5 \, \text{g/dL}$ or $11.3 \, \text{g/dL}$. The primary endpoint was a composite of death, MI, hospitalization for congestive heart failure, or stroke. The study was also prematurely stopped for futility after an interim analysis at a median study duration of 16 months because it was considered unlikely that benefit would be demonstrated for the primary composite cardiovascular endpoint. In fact, there were 125 events among 715 subjects in the high-Hb group vs. 97 events among 717 subjects in the low-Hb group (hazard ratio [HR], 1.34; 95% CI, 1.03 to 1.74; P = 0.03), with death and hospitalization for heart failure accounting for 75% of the events.

The CREATE study [6] in 603 patients with CKD stages 3–5 (26% with diabetes) failed to demonstrate the superiority of full anemia correction (Hb target 13.0 to 15.0 g/dL) with respect to cardiovascular events, as compared to partial correction of anemia (Hb target 11.0 to 12.5 g/dL), when starting ESA therapy at an earlier stage than ESRD.

Subsequently, TREAT, by far the largest trial, examined cardiovascular and kidney outcomes in 4038 patients with Stage 3 and 4 CKD [7]. TREAT was the only large placebo-controlled study to assess cardiovascular outcomes. Patients received either darbepoetin-alfa to achieve a Hb target of $13.0 \, \text{g/dL}$ or matching placebo with rescue darbepoetin-alfa when the Hb concentration was < $9.0 \, \text{g/dL}$. The HR for the first co-primary endpoint, the composite of death or a cardiovascular event, was $1.05 \, \text{(p=NS)}$. The HR for the second co-primary endpoint, death or ESRD, was $1.06 \, \text{(p=NS)}$. There was, however, a nearly two-fold increased risk of stroke (HR 1.92; $95\% \, \text{Cl} \, 1.38-2.68$) in the higher vs. lower Hb group, in patients both with and without a past history of stroke. In addition, venous thromboembolic events occurred significantly more frequently in the high Hb arm (2.0%) compared to the placebo arm (1.1%, p=0.02).

Based on these clinical trial data and safety surveillance, the ESA labeling was revised again to include the aforementioned warnings.

The international 2012 Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Evaluation and Management of Anemia of Chronic Kidney Disease [8] recommends addressing all correctable causes of anemia (including iron deficiency and inflammatory states) prior to initiation of ESA therapy. The guideline recommends balancing the potential benefits of reducing blood transfusions and anemia-related symptoms against the risks of harm in individual patients (e.g., stroke, vascular access loss, hypertension) (1B). For adult patients with NDD-CKD and Hb concentration < 10.0 g/dL, the decision whether to initiate ESA therapy can be individualized based on the rate of fall of Hb concentration, prior response to iron therapy, the risk of needing a transfusion, the risks related to ESA

therapy, and the presence of symptoms attributable to anemia (2C). For adult patients with NDD-CKD and Hb concentration \geq 10.0 g/dl, ESA therapy is not recommended (2D). For adult patients with CKD stage 5 on dialysis, ESA therapy is recommended when the Hb is between 9.0 and 10.0 g/dL (2B), and the KDIGO Guideline advises against use to maintain Hb above 11.5 g/dL (2C).

Hypoxia-inducible Factor Prolyl Hydroxylase Inhibitors

Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIFPHIs) represent a new class of orally administered ESAs. The applicant states the following in the Mechanism of Action section of their proposed roxadustat label:

"Through the inhibition of HIF-PH, roxadustat stimulates a coordinated erythropoietic response that includes the increase of plasma endogenous erythropoietin (EPO) levels, regulation of iron transporter proteins and reduction of hepcidin. This results in improved iron bioavailability, increased hemoglobin production and increased red cell mass."

The applicant hypothesizes that by avoiding the undesirable effects of excess exogenous erythropoietin, roxadustat may have advantages over currently available ESAs, beyond the convenience of an oral dosing form.

Commentary for the Committee

Erythropoiesis stimulating agents are indicated to treat the anemia of CKD based on their ability to increase Hb; however, clinical benefits (i.e., improvements in how patients feel, function, or survive) have not been demonstrated in adequate and well controlled trials. The anemia of CKD has been associated with decreased energy, well-being, and quality of life, as well as cognitive impairment. Although ESAs have been purported to improve these parameters, adequate and well controlled trials have not borne this out. As noted above, sizable randomized trials have attempted to demonstrate that use of ESAs to raise Hb to higher targets improves clinical outcomes, but instead, all have shown (or tended to show) adverse cardiovascular outcomes, leading to limitations on Hb targets as well as a boxed warning, the highest level of warning in product labeling.

ESAs can reduce the need for RBC transfusions, a clear benefit. Although the direct risks of transfusion are now rare (blood-borne infections, transfusion reactions, fluid overload), transfusion avoidance is particularly important in the ESRD population. Importantly, RBC transfusions can cause allosensitization that increases the likelihood of transplant rejection.

The cost of reduced RBC transfusions can be sizable. When ESAs are used to target excessive Hb concentrations, they increase the risk of death, MI, stroke, congestive heart failure, thrombosis of vascular access, and other thrombotic events. They can also cause hypertension and seizures. ESAs also carry warnings for shortened overall survival and increased risk of tumor progression/recurrence in patients with certain malignancies. Given that all of the Hb targeting studies have shown increased cardiovascular risks with higher, rather than lower, Hb targets, it might be assumed that these risks can be reduced by targeting lower Hb values, but it is not known if they can be <u>prevented</u> at <u>any</u> Hb target. No study has identified the optimum Hb target.

In light of these concerns, in 2010, FDA asked the Cardiovascular and Renal Drugs Advisory Committee to opine on whether ESA's indication for the treatment of anemia should be withdrawn in the NDD

patient population. Votes were strongly in favor of continued marketing: 1 "yes," 15 "no," and 1 abstention.

Roxadustat is a first-in-class inhibitor of HIF-PH enzymes. By reducing exposure to intermittent supraphysiologic doses of erythropoietin and improving iron metabolism and availability, the drug was hoped to achieve efficacy at least comparable to ESAs, with fewer safety issues. Moreover, the agent's oral route of administration is unquestionably an important convenience factor for patients who are not on hemodialysis. For patients on hemodialysis, ESAs are recommended to be given by the intravenous route, and the advantage of an oral preparation seems less obvious.

You will discover that roxadustat's efficacy is comparable to that of ESAs; however, there are important risks of serious thromboembolic events, as well as other risks, with roxadustat. Thus, both ESAs and roxadustat have pro-thrombotic effects. This observation raises important questions for discussion. First, how should roxadustat's risks be considered in the context of its benefits? Second, what are the causes of the thrombotic risk that is now observed across classes, and what are the contributing factors? It may help to revisit the questions that arose from the Hb targeting studies [9]. Is the thrombotic risk an on-target effect, mediated through effects on RBC production and related factors, or is it an off-target effect? If the risks are an on-target effect, they may be related to excess Hb concentration, Hb overshoots, excessive rates of Hb rise, rapid fluctuations in Hb, and changes in blood viscosity or volume. Although off-target effects cannot be ruled out, none are known, and, if such effects exist, they must be related to erythropoietin, whether given exogenously (in the case of ESAs) or stimulated indirectly (in the case of roxadustat). Assuming the thrombotic risk is an on-target effect, it seems plausible that less aggressive dosing schemes (e.g., lower starting doses, smaller dose increments during titration, lower Hb targets) could reduce thrombotic risk; however, this has not been established in any randomized controlled study.

We conducted exploratory analyses to elucidate associations between thromboembolic events and roxadustat dose, Hb concentrations, and Hb rates of rise and decline, identical to those undertaken in FDA's 2001 review of the darbepoetin alfa marketing application [10]. In this case, we asked the applicant to corroborate our findings, and they were able to do so. Indeed, higher rates of Hb rise (and decline) were found to be associated with higher rates of thromboembolic events. In light of these findings, the applicant speculates that thromboembolic risks might be reduced through use of a lower roxadustat starting dose. Their prediction seems plausible, but is unproven. Our findings show only associations, without proven cause and effect.

FDA's approval standards state that drugs must be both effective and safe to be approved. Our standards do not state that a drug must be more effective than existing treatment(s) to merit approval, or be safer than existing treatments. Yet when weighing the approval of a new drug, we do consider its benefits and risks in context, including the availability of other therapies. The benefits are difficult to calculate here. The data show that roxadustat decreases the need for RBC transfusions relative to placebo, which is expected and reassuring. The data comparing roxadustat to epoetin alfa with respect to RBC transfusions are less conclusive. And if one believes that the risk of thromboembolic events is greater with roxadustat than ESAs, a critical question is whether lowering the roxadustat starting dose will reduce risk importantly.

The applicant makes the case that ESA hyporesponsiveness in patients with CKD is an important problem in need of better therapies. We agree with this viewpoint; however, the applicant did not generate data showing that patients who are hyporesponsive to ESAs are responsive to roxadustat.

Finally, we note that the roxadustat development program was carried out in two distinct patient populations, with important differences. In the dialysis population, subjects were randomized to roxadustat or epoetin alfa, and subject retention was similar with both treatments. Overall exposure differed by ~11%. Thus, for the purpose of safety analyses, the correction needed for disparate time on study was relatively small, and interpretation of the results of safety analyses is clear-cut.

In the NDD patient population, the applicant carried out placebo-controlled studies in patients who were anemic at baseline, with the possibility of "rescue" therapy if needed. These placebo-controlled studies had the advantage of assessing the safety of roxadustat against a "clean" background; however, many subjects dropped out of the studies, and data from these subjects cannot be considered 'missing at random.' Patients with more advanced disease whose Hb was poorly responsive to the study drug were more likely to leave the study, and experience has shown that such patients are at greater risk of cardiovascular events. As patients who received placebo were more likely to remain anemic, they were more likely to drop out of the study than patients who received roxadustat. Thus, there was a considerable disparity in subject retention between the roxadustat and placebo groups, challenging the interpretation of safety analyses. It seems plausible that the patients who dropped out of the placebo groups in higher numbers were at greater risk of adverse events, yet their time of observation—when they were capable of contributing adverse events—was shortened. Conversely, subjects randomized to roxadustat remained in the studies longer, with greater opportunity to experience adverse events.

Given the above, the assessment of adverse events in the NDD subject population is not straightforward. The results of the analyses depend on how the data were analyzed; specifically, whether the time of observation was limited to the time on-treatment (plus 7 days), extended to last contact (on-study analysis), or truncated at a point between these extremes (e.g., on-treatment plus 28 days). These considerations affect all of the safety analyses, including analyses for MACE.

Draft Points to Consider

The applicant is seeking approval of roxadustat, an oral agent for treatment anemia due to CKD, in adult patients not on dialysis and on dialysis.

Non-dialysis-dependent population:

- 1. Discuss the benefits and risks of roxadustat in the non-dialysis-dependent (NDD) population.
- 2. If you have concerns regarding these risks, discuss whether you believe they could be addressed through modification of the treatment algorithm, for example, changes in target hemoglobin (Hb), starting dose, titration scheme, monitoring paradigm.
 - a. If you favor changes to the treatment algorithm to enhance safety, should they be tested prior to approval?

Dialysis population:

3. Discuss the benefits and risks of roxadustat in the dialysis-dependent (DD) population.

- 4. If you have concerns regarding these risks, discuss whether you believe they could be addressed through modification of the treatment algorithm, for example, changes in target Hb, starting dose, titration scheme, monitoring paradigm.
 - a. If you favor changes to the treatment algorithm to enhance safety, should they be tested prior to approval?
- 5. Should roxadustat be approved for treatment anemia due to CKD, in adult patients not on dialysis?
 - a. If not, provide your rationale, as well as recommendations for additional data and/or analyses that would support a favorable benefit-risk profile and approval of roxadustat.
- 6. Should roxadustat be approved for treatment anemia due to CKD, in adult patients on dialysis?
 - a. If not, provide your rationale, as well as recommendations for additional data and/or analyses that would support a favorable benefit-risk profile and approval of roxadustat.

Evidence of Efficacy

Roxadustat's evidence of effectiveness for the treatment of anemia due to CKD in adult patients is based primarily on six adequate and well-controlled trials.

Non-dialysis dependent (NDD) population: principal studies included three randomized, placebocontrolled, double-blind studies:

- 1517-CL-0608/ALPS (henceforth referred to as "608" in this document)
- FGCL-4592-060/ANDES (referred to as "060" in this document)
- D5740C00001/OLYMPUS (referred to as "001" in this document)

Study 1517-CL-0610/DOLOMITES (referred to as "610" in this document) differed from those above because it employed an active comparator (darbepoetin alfa), was not double-blind, and was conducted solely in Eastern and Western Europe. The study was ongoing at the time the applicant submitted the New Drug Application, and we received the clinical study report early in the review period.

Dialysis-dependent (DD) population: principal studies included 3 randomized, active-controlled (epoetin alfa), open-label studies:

- FGCL-4592-063/HIMALAYAS (referred to as "063" in this document)
- FGCL-4592-064/SIERRAS (referred to as "064" in this document)
- 5740C00002/ROCKIES (referred to as "002" in this document)

Study 1517-CL-0613/PYRENEES (referred to as "613" in this document) provides supplemental information; the study differs from those above because it employed two active comparators (darbepoetin alfa and epoetin alfa), was conducted exclusively in Europe, and permitted use of an ESA that is not licensed in the US.

In light of the safety concerns of the ESAs, the Division has asked sponsors to assess MACE in development programs for drugs for the treatment of anemia of CKD, in both the NDD and DD populations, as noted above. For the NDD indication, studies 608, 001, and 060 were included in a meta-analysis for MACE. For the DD indication, studies 002, 063 and 064 were included in a MACE meta-analyses. Trials 610 and 613 were not considered sufficiently similar to the others to allow inclusion in the meta-analyses.

NDD Indication

Study Designs

The Phase 3 studies for the NDD population are summarized in Table 2. All were multicenter (global), randomized, controlled studies that evaluated the efficacy of roxadustat in correcting Hb. All patients had stage III to V CKD with baseline eGFR < $60 \text{ mL/min/1.73 m}^2$. The primary efficacy endpoint for the US was the mean Hb change from baseline to the mean level during the evaluation period, defined as Week 28 until Week 52. The proportions of subjects with RBC transfusions was a secondary endpoint.

Table 2: Major Trials in the NDD Population

_	Placebo-controlled			ESA-controlled
Design Feature				
	Study 001	Study 060	Study 608	Study 610
Blinding	Double-blind	Double-blind	Double-blind	Open-label
Control	Placebo	Placebo	Placebo	Darbepoetin
Planned Treatment Duration (weeks)	52 - 208	52 - 208	52 - 104	104
Number of Patients	2761	922	594	616
Randomization	1:1	2:1	1:1>2:1	2:1> 1:1
Baseline Hb (g/dL)	< 10.0	≤ 10.0	≤ 10.0	≤ 10.5
Hb target - Correction Period (g/dL)	11.0 ± 1.0	\geq 11.0 and \geq 1.0 from baseline	\geq 11.0 and \geq 1.0 from baseline	\geq 11.0 and \geq 1.0 from baseline
Hb target - Maintenance Period (g/dL)	10.0 - 12.0	10.0 - 12.0	10.0 - 12.0	10.0 - 12.0
Roxadustat starting dose				
(dose given 3 times/week)				
body weight < 70 kg:	70 mg	70 mg	70 mg	70 mg
body weight > 70 kg:	70 mg	100 mg	100 mg	100 mg

Patients with New York Heart Association Class III or IV congestive heart failure (CHF) at enrollment, and patients who had an MI, acute coronary syndrome, stroke, seizure, or a thromboembolic event within 12 weeks prior to randomization were excluded. Patients with uncontrolled hypertension were also excluded. The trials had recommendations for rescue therapy (i.e., iron, ESAs, or transfusion).

The algorithm for dosage adjustments is shown in Table 3. Adjustment was based on the Hb level and the change in Hb over the previous 4 weeks.

Table 3: Roxadustat Dose Adjustment Algorithm for NDD-CKD Subjects

Change in Hb	C				
over Past 4 weeks (g/dL) Correction Period*	Hb < 10.5 g/dL	Hb 10.5-11.9 g/dL	Hb 12.0-12.9 g/dL	Hb≥13.0 g/dL	
<-1.0	1	1	<u> </u>	No change	Hold dosing, check Hb and resume
-1.0 to 1.0	1	1	No change	↓	dosing when Hb <12.0 g/dL, at a dose that is reduced by two dose steps
> 1.0	No change	No change	↓	↓	

Abbreviations: \uparrow = dose increase; \downarrow = dose reduction; Hb = hemoglobin

Source: FibroGen Summary of Clinical Efficacy p. 147

Dose increases and reductions:

- Roxadustat dose increases (\uparrow) and reductions (\downarrow) were intended to be preset according to dose steps: 20, 40, 50, 70, 100, 150, 200, 250, and 300 mg. For example, a dose increase at 70 mg would result in a new dose of 100 mg. A dose reduction at 200 mg would result in a new dose of 150 mg.
- The suggested maximum dose was 3.0 mg/kg or 300 mg per administration, whichever was less.

Dose adjustment for rapid Hb increase:

- For Hb increases >2.0 g/dL in 4 weeks, the dose was to be reduced by one dose step immediately.
- Only one dose reduction for rapid Hb increase was recommended within a 4-week period.

Results

Demographic and Baseline Characteristics: Demographic and baseline disease characteristics were generally well balanced between the two treatment groups for the three trials. The mean age of patients was approximately 63 years. Twenty-one percent of patients were age 75 or greater. A majority of the patients were female (58%). Approximately half the patients were Caucasian, 8% were Black, and 36% were Asian. Most were not on prior ESA treatment. Approximately one-quarter of patients were from the US. More than one-third of patients had a history of cardiovascular, cerebrovascular, or thromboembolic disease. More than 90% of trial participants reported hypertension, and diabetes mellitus was reported as a baseline condition by 37% to 65% of trial participants. The baseline Hb was 9.1 g/dL in both treatment groups. The mean eGFR at baseline was approximately 20 mL/min/1.73 m² for all studies.

Table 4: Selected Demographics and Baseline Disease Characteristics—NDD Trials

Trial	0	01	060		60	8
Characteristic	Roxadustat (N=1384)	Placebo (N=1377)	Roxadustat (N=616)	Placebo (N=306)	Roxadustat (N=391)	Placebo (N=203)
Age in years mean (SD)	60 9 (14.7)	62.4 (14.1)	64.9 (12.6)	64.8 (13.2)	60.6 (13.5)	61.7 (13.8)
Female, n (%)	820 (59.2)	774 (56.2)	375 (60 9)	176 (57 5)	222 (56.8)	104 (51.2)
Race, n (%)						
White	623 (45.0)	611 (44.4)	176 (28.6)	99 (32.4)	335 (85.7)	182 (89.7)
Black	112 (8.1)	115 (8.4)	76 (12.3)	28 (9.2)	10 (2.6)	3 (1.5)
Asian	544 (39.3)	539 (39.1)	310 (50 3)	151 (49 3)	9 (2.3)	0 (0)
Native Hawaiian or other Pacific Islander	0 (0)	2 (0.1)	2 (0.3)	4 (1.3)	NR	NR
American Indian or Alaska Native	24 (1.7)	29 (2.1)	6 (1.0)	1 (0.3)	NR	NR
Other	81 (5.9)	82 (6.0)	46 (7.5)	23 (7.5)	37 (9.5)	18 (8.9)
Ethnic Group, n (%)						
Hispanic or Latino	344 (24.9)	357 (25.9)	165 (26.8)	84 (27.5)	NR	NR
eGFR (mL/min/1.73m ²) (SD)	19.7 (11.7)	20.0 (11.7)	21.9 (11.5)	22.4 (11.4)	16.5 (10.2)	17 2 (11.7)
Hb Mean (SD)	9.11 (0.73)	9.10 (0.74)	9.10 (0.75)	9.09 (0.69)	9.08 (0.76)	9.10 (0.72)
Prior ESA use, n (%)	15 (1.1)	13 (0.9)	130 (21 3)	48 (15.7)	45 (11.5)	24 (11.8)
Iron Replete, n (%)	809 (58.5)	799 (58.0)	373 (60.6)	170 (55.6)	204 (52.2)	109 (53.7)
Diabetes, n (%)	793 (57.3)	807 (58.6)	395 (64.6)	199 (65 2)	146 (37.3)	89 (43.8)
Cardiovascular disease, n (%)	410 (29.6)	420 (30.5)	210 (34.4)	101 (33.1)	141 (36.1)	89 (43.8)
Cerebrovascular disease, n (%)	105 (7.6)	120 (8.7)	81 (13.3)	39 (12.8)	26 (6.6)	20 (9.9)
Thromboembolic disease, n (%)	30 (2.2)	22 (1.6)	11 (1.8)	3 (1.0)	9 (2.3)	2 (1.0)

Patient Disposition and Discontinuation: For the three studies overall, 62% and 41% of patients randomized to roxadustat and placebo, respectively, completed the treatment period. Decisions to withdraw by either the patient or physician accounted for approximately half of all discontinuations in both groups (Table 5). Discontinuation for ESA rescue therapy was ~4 times higher in patients who received placebo (13.4%) than in roxadustat-treated patients (3.2%). The percentage of patients who discontinued in association with an adverse event(s) was higher among patients treated with roxadustat (6.3%) than in subjects randomized to placebo (4.4%). Deaths were also more frequent in patients randomized to roxadustat (3.4%) than in those randomized to placebo (1.6%).

Table 5: Patient Disposition (NDD Safety Population)

N (%)	Roxadustat (N=2386)	Placebo (N=1884)
Intent-to-treat population	2391	1886
Treated patients	2386 (99.8)	1884 (99.9)
Completed treatment	1485 (62.2)	769 (40.8)
Discontinued treatment early	901 (37.8)	1115 (59.2)
Adverse events	150 (6.3)	83 (4.4)
Death	81 (3.4)	30 (1.6)
Received > 2 courses of ESA rescue therapy	76 (3.2)	252 (13.4)
Lost to follow-up	33 (1.4)	74 (3.9)
Dialysis initiation or kidney transplant	47 (2.0)	20 (1.1)
Physician decision	49 (2.1)	67 (3.6)
Subject decision	250 (11.0)	390 (20.7)
Withdrawal by subject or guardian	144 (6.1)	144 (7.7)
Other	71 (2.9)	55 (2.9)

Drug Exposure: Overall, the duration of study drug exposure was greater in patients treated with roxadustat (mean 84.6 weeks per patient; total 3871 patient-years) than in patients who received placebo (mean 64.3 weeks per patient; total 2323 patient-years). Approximately 71% of roxadustat-treated patients received the drug for > 52 weeks and 34% received it for > 104 weeks. The applicant attributed the higher overall drug exposure in roxadustat-treated patients to the 2:1 randomization ratio (roxadustat:placebo) in the two smaller studies (060 and 608) and the higher dropout rate in patients who received placebo, mainly due to lack of efficacy in all three studies.

Primary Endpoint

As noted above, the primary endpoint in the three principal studies was the mean change in Hb from baseline to the evaluation period (mean value during Weeks 28-52), regardless of rescue therapy, using the intention-to-treat (ITT) analysis set. Efficacy analyses were performed separately for each study. Roxadustat would be considered superior to placebo if the difference in the mean change from baseline between the two treatment groups was statistically significant (p < 0.05) using a multiple imputation analysis of covariance (ANCOVA) method. All three studies demonstrated statistically significant results with respect to change in Hb, and FDA was able to corroborate the applicant's findings (Table 7).

Table 6: Drug Exposure in NDD Population

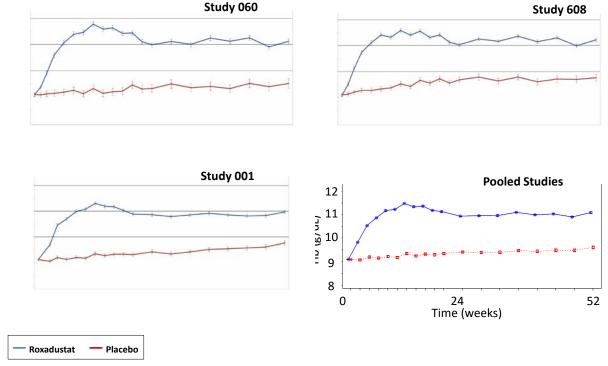
Roxadustat	Placebo
(N=2386)	(N=1884)
84.6 (48.8)	64.3 (44.8)
87.1 (0, 235)	57.1 (0, 208)
3870.7	2323.2
2263.1	1747.6
1134.9	377.3
472.7	198.3
86 (3.6)	81 (4.3)
2300 (96.4)	1803 (95.7)
2020 (84.7)	1389 (73.7)
1694 (71.0)	1005 (53.3)
812 (34.0)	397 (21.1)
(N=481)	(N=358)
72.3 (50.2)	47.8 (41.2)
67.7 (0, 216)	32.3 (0, 164)
	(N=2386) 84.6 (48.8) 87.1 (0, 235) 3870.7 2263.1 1134.9 472.7 86 (3.6) 2300 (96.4) 2020 (84.7) 1694 (71.0) 812 (34.0) (N=481) 72.3 (50.2)

Table 7: Efficacy Endpoints for NDD Trials

Trial/Treatment Arm	00	1	06	50	608		
	Roxadustat	Placebo	Roxadustat	Placebo	Roxadustat	Placebo	
	N=1384	N=1377	N=616	N=306	N=391	N=203	
Mean baseline Hb (SD)	9.11 (0.73)	9.10 (0.74)	9.10 (0.75)	9.09 (0.69)	9.08 (0.76)	9.10 (0.72)	
Mean Hb Week 28–52	10.84 (0.86)	9.50 (1.18)	11.10	0.25 (1.06)	11 16 (0.94)	0.60/1.02\	
(SD)	10.64 (0.66)	9.50 (1.16)	(0.70)	9.25 (1.06)	11.16 (0.84)	9.60 (1.02)	
Hb change from							
baseline to average Hb	1.75 (0.03)	0.40 (0.03)	2.00 (0.95)	0.16 (0.89)	1.99 (0.95)	0.41 (0.98)	
in Weeks 28 to 52 (SE)							
Least squares mean							
(LSM) difference	1.35 (1.2	27, 1.43)	1.85 (1.	74, 1.97)	1.69 (1.5	2, 1.86)	
roxadustat from	P < 0	.001	P < 0	.0001	P < 0.001		
placebo (95% CI)							
Subjects with RBC	176 (12.7)	320 (23.3)	34 (5.6)	47 (15.4)	33 (8.5)	39 (19.2)	
transfusions, N (%)	170 (12.7)	320 (23.3)	34 (3.0)	47 (13.4)	33 (8.3)	33 (13.2)	
Hazard Ratio; Nominal	0.37: <	0.37; < 0.001		0.26; < 0.001		0.34; < 0.001	
P-value	0.57,		0.20,	- 0.001	0.54,	3.301	

Figure 1 shows the results graphically for the three individual studies as well as the pooled studies. On average, the Hb appears to plateau at target at approximately 12 weeks (~8 weeks in study 608).

Figure 1: Changes in Hb over Time—NDD Studies



Source: FDA analysis

Study 610

Study 610 was a multicenter, European, randomized, controlled trial in patients with NDD-CKD. The study differed from the others in that there was an active comparator (darbepoetin alfa), the study was open-label, and the study was conducted exclusively in Europe. The randomization scheme was initially 2:1 (version one of protocol) but changed to 1:1 (version two).

The starting roxadustat dose was 70 mg for body weight < 70 kg and 100 mg for body weight \geq 70 kg three times a week. Dose titration was conducted based upon the Hb target of 11 ± 1 g/dL. Darbepoetin alfa was dosed subcutaneously or intravenously according to the EU labeling.

The primary efficacy endpoint was the percentage of Hb responders during the first 24 weeks of treatment. A responder was defined as a subject who attained a Hb response as follows:

- Hb≥11.0g/dL and an increase from baseline ≥ 1.0g/dL (subjects with baseline Hb > 8.0g/dL); or
- An increase from baseline $\geq 2.0 \,\text{g/dL}$ (subjects with baseline Hb $\leq 8.0 \,\text{g/dL}$)

Patients receiving rescue therapy were non-responders.

Noninferiority was to be declared if the lower bound of the two-sided 95% CI was > -15%. The primary endpoint was to be analyzed using the Per Protocol Analysis set, consisting of all randomized patients who received \geq 1 dose of study drug, had \geq 1 post-dose Hb assessment, and did not meet any exclusion criteria.

Demographic and baseline disease characteristics were comparable between the two treatment groups (Table 8). Mean age was 66 years. The majority of patients were Caucasian (95%), and approximately 56% were women. Approximately 30% were from Western Europe, with 70% from Eastern Europe. In both treatment groups, the mean baseline Hb was $9.55 \, \text{g/dL}$ and the mean baseline eGFR was $20.3 \, \text{mL/min/1.73 m}^2$. Just under half of all patients had a history of cardiovascular, cerebrovascular, or thromboembolic disease.

Table 8: Selected Demographic and Baseline Disease Characteristics—Study 610

	Treatment Groups		
	Roxadustat (N=323)	Darbepoetin (N=293)	
Age in years mean (SD)	66.8 (13.6)	65.7 (14.4)	
Female, n (%)	178 (55.1%)	164 (56.0%)	
Race, n (%)			
Caucasian	306 (94.7%)	281 (95.9%)	
Black	8 (2.5%)	2 (0.7%)	
Asian	9 (2.8%)	10 (3.4%)	
Baseline eGFR (mL/min/1.73m²) (SD)	20.3 (11.5)	20.3 (10.7)	
Baseline Hb mean (SD)	9.55 (0.75)	9.55 (0.69)	
Baseline iron replete, n (%)	182 (56.3%)	152 (51.9%)	
Diabetes, n (%)	150 (46.5%)	137 (46.7%)	
History of cardiovascular,			
cerebrovascular, or thromboembolic	152 (47.1%)	142 (48.5%)	
disease, n (%)			

Patient Disposition and Discontinuations

Study retention was similar in the two treatment groups: 22.9% of patients in the roxadustat group vs. 19.8% in the darbepoetin alfa group withdrew before the Week 24 cutoff. The most frequent reasons for discontinuation in the roxadustat group were withdrawal by patient (9.9%), death (8.4%), and adverse events (6.5%). The most common reasons for discontinuation in the darbepoetin group were death (10.2%), withdrawal by patient (6.8%), and adverse event (2.7%).

Efficacy Endpoint

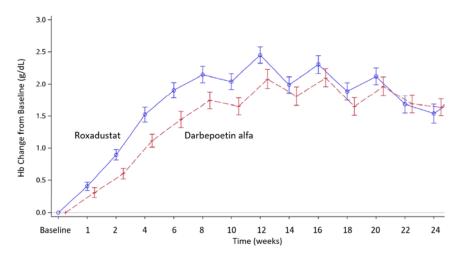
For the per-protocol analysis set, 89.5% of patients in the roxadustat group vs. 78.0% in the darbepoetin alfa group were responders (Table 9). The difference in proportions was 11.5%, favoring roxadustat, and the 95% CI of the response rate difference excluded -15%, meeting the study's efficacy objective.

The changes in Hb are shown graphically in Figure 1. Although the rate of Hb rise was not evaluated as a study endpoint, a trend showing more rapid Hb increase in the roxadustat group is clearly evident, which may have ramifications for safety.

Table 9: Efficacy Results for Trial 610 (Ns Represent Numbers in the Per-protocol Analysis Set)

	Roxadustat	Darbepoetin alfa	
	N=286	N=272	
Number of responders	256 (89.5%)	213 (78.0%)	
95% CI	(85.4%, 92.8%)	(72.6%, 82.8%)	
Difference of proportions (roxadustat – darbepoetin alfa)	11.5%		
95% CI of difference	(5.66%, 17.36%)		

Figure 2: Hb Change from Baseline by Time (mean ± 95% CI)—Study 610 (figure adapted from applicant)



DD Population

Study Designs

Roxadustat's efficacy for the treatment of anemia in adult patients with DD-CKD is supported by three randomized, active controlled, non-inferiority trials: 002, 063, and 064. These were similarly designed, open-label studies where subjects were randomized 1:1 to roxadustat or epoetin alfa. All subjects had Stage 3 to 5 CKD with a baseline Hb level < 10 g/dL (if not on an ESA) or < 12 g/dL (if on an ESA). All trials excluded patients with New York Heart Association Class III or IV CHF at enrollment, and patients with a history of MI, acute coronary syndrome, stroke, seizure, or thrombotic event within 12 weeks prior to enrollment. Patients with uncontrolled hypertension were also excluded. The intended duration was ≥ 52 weeks. The trials had recommendations for rescue therapy using ESAs or transfusion in the roxadustat group and transfusion in the epoetin alfa group. The roxadustat dose was titrated to achieve a Hb target of 10.0 to 11.0 g/dL in the US and 10.0 to 12.0 g/dL outside the US. The primary endpoint for the three studies was the mean change in Hb from baseline to Weeks 28 to 52, regardless of rescue therapy. Having determined the mean treatment effect in both groups, non-inferiority (NI) of roxadustat to epoetin alfa was to be declared if the lower bound of the 95% CI of the inter-group difference

(roxadustat - epoetin alfa) was greater than the pre-defined NI margin -0.75 g/dL, i.e., the 95% CI excluded a difference of 0.75 g/dL or more. The proportions of subjects with RBC transfusions was a secondary endpoint. Major design features are summarized in Table 10.

Study 002 enrolled patients with ESRD who were receiving, or had initiated, hemodialysis or peritoneal dialysis at least 30 days prior to enrollment. Amendment #6, designed to increase enrollment of US patients with incident dialysis, changed the dialysis criterion to receiving at least 2 weeks and not more than 4 months. At enrollment, subjects could be on an ESA (with Hb <12.0 g/dL) or not on an ESA (with Hb <10 g/dL). For patients not on an ESA, the roxadustat starting dose was 70 mg orally thrice weekly regardless of body weight; for patients on an ESA, the starting dose was calculated on the basis of the ESA dose (range: 70 to 200 mg thrice weekly).

Study 063 enrolled patients with CKD and incident dialysis (2 weeks to 4 months prior to randomization), with baseline Hb \leq 10 g/dL. The roxadustat starting dose was 70 mg for body weight < 70 kg and 100 mg for body weight \geq 70 kg, thrice weekly.

Study 064 enrolled subjects who were on a stable ESA dose \geq 4 weeks prior to and during screening, with an allowable Hb range of 8.5 to 12.0 g/dL. Amendment #1 and #2 encouraged the enrollment of more patients considered to have incident dialysis as defined for Study 063. The starting roxadustat dose was 70 to 200 mg thrice weekly, calculated on the basis of the prior ESA dose.

Only Study 063 enrolled exclusively incident dialysis. The other studies amended their protocols to enroll incident dialysis and planned to later compare results between incident and stable dialysis subgroups. Incident dialysis did not have a standard definition. Because of the multiple amendments and lack of a standardized definition, FDA did not further analyze this subgroup.

Study 613, described separately, was conducted in Eastern, Central, and Western Europe, and used both darbepoetin alfa and epoetin alfa as comparators. Use of an ESA, approved in the EU but not licensed in the US, was permitted.

Table 10: Major Trials in the DD Patient Population

		Major Studies		Supportive Study
Design Feature	Study 002	Study 063	Study 064	Study 613
Blinding	Open-label	Open-label	Open-label	Open-label
Control	Epoetin alfa	Epoetin alfa	Epoetin alfa	Epoetin alfa/ darbepoetin alfa
Planned treatment duration (years)	< 4	< 4	< 4	1 - 2
Number of Patients	2106	1043	741	836
Randomization	1:1	1:1	1:1	1:1
Baseline Hb (g/dL)	< 10.0 ‡; <12.0	≤ 10.0	9.0 † to 12.0	9.5 to 12.0
Stable dialysis (SD); incident dialysis (ID); dialysis-dependent (DD)	SDD and ID-DD	ID-DD	SDD and ID-DD	SDD
Hb target - Maintenance Period (g/dL)	10.0 - 12.0 §	10.0 - 12.0 §	10.0 - 12.0 §	10.0 - 12.0
Hb correction or conversion	Correction and conversion	Correction	Conversion	Conversion

 $[\]dagger \geq 8.5 \, \text{g/dL}$ for ID-DD patients; \ddagger For subjects not on an ESA

Dosage adjustment was based on the Hb level and the change in Hb over the previous 4 weeks, and was the same for all three studies (Table 11).

Table 11: Roxadustat Dosage Adjustment for Studies 063, 064, and 002

Changes in Hb over past 4 weeks	Hb <10.5 g/dL	Hb 10.5 to 11.9 g/dL	Hb 12.0 to 12.9 g/dL	Hb ≥13.0 g/dL
<-1.0	↑	↑	No change	Dose withheld and
-1.0 to 1.0	1	No change	↓	resumed when Hb was ≤11.9 g/dL, at a dose that
>1.0	No change	\	\	was to be reduced by 2 dose steps

Source: Modified FibroGen Table 6 from Clinical Study Report for Study 002

Results

Demographics & Baseline Disease Characteristics

The demographics and baseline disease characteristics for all three trials were generally balanced between the two groups. Overall, approximately 45% of patients were enrolled in US sites. Meanage

 $[\]S$ 10.0 to 11.0 g/dL in the US; 10.0 to 12.0 g/dL outside the US

ID-DD = incident dialysis; SDD = stable dialysis-dependent

was 54 to 58 for all studies. At baseline, most patients were male (58%), White (varied by study), on prior ESA treatment, and on stable dialysis. Study 064 was conducted solely in the US, and 42% of participants were Black. More than 90% of trial participants reported hypertension as a baseline medical condition. Diabetes mellitus was reported as a baseline condition by 28% to 65% of trial participants. Overall, about half of the subjects had a history of cardiovascular, cerebrovascular, or thromboembolic disease. The mean baseline Hb was similar between the two groups, averaging 9.6 g/dL over the three studies. Overall, approximately, 90% of patients in both treatment groups were receiving hemodialysis, and the rest were receiving peritoneal dialysis.

Table 12: Selected Demographics and Baseline Disease Characteristics for DD Trials

Trial	0	02	0	53	064	
Characteristic	Roxadustat (N=1051)	Epoetin alfa (N=1055)	Roxadustat (N=522)	Epoetin alfa (N=521)	Roxadustat (N=370)	Epoetin alfa (N=371)
Age mean (SD) (years)	53.5 (15.3)	54 5 (15.0)	53.8 (14.7)	54.3 (14.6)	57.6 (13.6)	58.4 (13.3)
Female, n (%)	426 (40.5)	429 (40.7)	213 (40.8)	214 (41.1)	183 (49.5)	156 (42.0)
Race, n (%)						
White	597 (56.8)	598 (56.7)	415 (79.5)	400 (76.8)	165 (44.6)	184 (49.6)
Black	148 (14.1)	158 (15.0)	44 (8.4)	50 (9.6)	158 (42.7)	156 (42.0)
Asian	208 (19.8)	198 (18.8)	43 (8 2)	51 (9.8)	21 (5.7)	15 (4.0)
Native Hawaiian or other Pacific Islander	5 (0.5)	3 (0.3)	NR	NR	1 (0.3)	3 (0.8)
American Indian or Alaska Native	50 (4.8)	62 (5.9)	1 (0.2)	4 (0.8)	10 (2.7)	7 (1.9)
Other	43 (4.1)	36 (3.4)	19 (3.6)	16 (3.1)	15 (4.1)	6 (1.6)
Hispanic or Latino	268 (25.5)	271 (25.7)	99 (19.0)	77 (14.8)	137 (37.0)	129 (34.8)
US subjects, n (%)	385 (36.6)	391 (37.1)	127 (24.3)	125 (24.0)	370 (100)	371 (100)
Hemodialysis, n (%)	938 (89.2)	938 (88.9)	469 (89.8)	462 (88.7)	354 (95.7)	354 (95.4)
Peritoneal Dialysis, n (%)	111 (10.6)	117 (11.1)	53 (10.2)	58 (11.1)	16 (4.3)	17 (4.6)
Dialysis Duration > 4 months, n (%)	852 (81.1)	841 (79.8)	2 (0.4)	2 (0.4)	334 (90.3)	336 (90.6)
Baseline Hb Mean (SD) (g/dL)	9.99 (1.20)	10.02 (1.24)	8.43 (1.04)	8.46 (0.96)	10.30 (0.66)	10.31 (0.66)
Diabetes, n (%)	459 (43.7)	454 (43.0)	205 (39.3)	204 (39.2)	250 (67.5)	255 (68.8)
History of cardiovascular, cerebrovascular, or thromboembolic disease, n (%)	305 (29.0)	304 (28.8)	219 (42.0)	224 (43.0)	229 (61.9)	210 (56.6)

Patient Disposition

Of 3890 patients randomized, 3880 were treated (roxadustat = 1940; epoetin alfa = 1940). Treatment completion rates were 58.5% and 66.3% in the roxadustat and epoetin alfa groups, respectively, and reasons for discontinuation are shown in Table 13. Discontinuations were disproportionately higher in the roxadustat group for adverse events, death, and the need for ESA rescue therapy.

Table 13: Patient Disposition DD Safety Population (002, 063, 064)

N (%)	Roxadustat	Epoetin Alfa
	(N=1940)	(N=1940)
Intent-to-treat population	1943	1947
Treated patients	1940 (99.8)	1940 (99.6)
Completed treatment	1135 (58.5)	1287 (66.3)
Discontinued treatment Early	805 (41.5)	653 (33.7)
Adverse events	110 (5.7)	54 (2.8)
Death	141 (7.3)	129 (6.6)
Received > courses of ESA rescue therapy	32 (1.6)	0 (0)
Kidney transplant	115 (5.9)	147 (7.6)
Subject decision	135 (7.0)	88 (4.5)
Withdrawal by subject or guardian	78 (4.0)	78 (4.0)
Physician decision	68 (3.5)	32 (1.6)
Lost to Follow-up	10 (0.5)	5 (0.3)
Others	116 (6.0)	120 (6.1)

Drug Exposure

Figure 3 shows the differential retention of subjects in the roxadustat and ESA groups for the three studies. As predicted by the figure, the mean duration of study drug exposure was shorter in patients randomized to roxadustat (89.2 weeks) than to epoetin alfa (100.7 weeks). Total durations of exposure were 3315 and 3744 patient-years, respectively. The percentages of patients who received the study drug through Week 52 (the end of the assessment period for the primary endpoint) were 63% for roxadustat and 71% for epoetin alfa.

Figure 3: Subject Retention for the DD Population—Studies 002, 063, 064

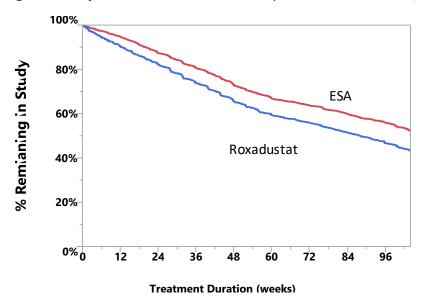


Table 14: Duration of Exposure in DD Population (002, 063, 064)

	Roxadustat (N = 1940)	Epoetin Alfa (N = 1940)
Duration of exposure (weeks)		
Mean (SD)	89.2 (58.6)	100.7 (57.5)
Median (min, max)	87.9 (0, 228)	107.5 (0, 227)
Duration of exposure, mean (years)	1.71	1.93
Exposure by study (patient-years)		
Total	3315.3	3743.6
Study 002	1800.1	2032.7
Study 063	890.7	759.3
Study 064	624.5	951.6
Exposure, n (%)		
≤ 4 Weeks	71 (3.7)	34 (1.8)
> 4 Weeks	1869 (96.3)	1906 (98.2)
> 26 Weeks	1572 (81.0)	1683 (86.8)
> 52 Weeks	1223 (63.0)	1370 (70.6)
> 104 Weeks	831 (42.8)	1010 (52.1)
> 156 Weeks	302 (15.6)	385 (19.8)

Primary Endpoint

All three studies demonstrated non-inferiority of roxadustat vs. epoetin alfa (Table 15), as the lower bound of the 95% CI of the treatment difference (roxadustat - epoetin alfa) exceeded the prospectively-defined NI margin of -0.75 g/dL. Statistically significantly fewer subjects received RBC transfusions in the roxadustat group than in the epoetin alfa group in Study 064; however, Studies 002 and 063 showed opposite trends (Table 15). Moreover, it is important to recognize that the transfusion data are confounded. Subjects who were randomized to roxadustat could receive ESAs or RBC transfusions as a rescue therapy, whereas subjects who were randomized to epoetin alfa could receive only a transfusion as rescue therapy. Thus, it cannot be concluded that subjects who received roxadustat required fewer RBC transfusions than subjects who received epoetin alfa.

Table 15: Efficacy Results for the DD Trials

	002		063		064		
Study/Treatment Arms	Roxadustat	Epoetin alfa	Roxadustat	Epoetin alfa	Roxadustat	Epoetin alfa	
	N=1051	N=1055	N=522	N=521	N=370	N=371	
Mean Baseline Hb (SD)	9.99 (1.2)	10.02 (1.24)	8.43 (1.04)	8.46 (0.96)	10.30 (0.66)	10.31 (0.66)	
Hb averaged over Weeks 28–52 (SD)	10.83 (0.94)	10.74 (1.02)	11.00 (0.82)	10.83 (0.88)	10.69 (0.76)	10.22 (0.68)	
Change from baseline in Hb average over Weeks 28 to 52 (adjusted mean) (SE)	0.77 (0.04)	0.68 (0.04)	2.38 (0.04)	2.20 (0.04)	0.28 (0.07)	-0.19 (0.06)	
Difference: Roxadustat minus Epoetin alfa (95% CI)	0.09 (0.0	0.09 (0.01, 0.18)		0.18 (0.08, 0.29)		0.48 (0.37, 0.59)	
Subjects with RBC transfusions, N (%)	103 (9.8)	139 (13.2)	38 (7.3)	33 (6.4)	46 (12.5)	78 (21.1)	
Hazard Ratio; Nominal P- value	0.83;	0.15	1.26;	0.33	0.67	; 0.04	

Study 613

Study 613 (Pyrenees) was a randomized, open-label, non-inferiority trial in patients with DD-CKD on stable hemodialysis or peritoneal dialysis for ≥ 4 months and on stable ESA treatment for ≥ 8 weeks. The study was conducted at multiple sites in Eastern, Central, and Western Europe. Patients were randomized 1:1 to roxadustat or continued treatment with their prior ESA: darbepoetin alfa or epoetin alfa. (Of note, randomization was not stratified by prior ESA.) Use of an ESA, approved in the EU but not licensed in the US, was permitted. Eligible patients were required to have a baseline Hb between 9.5 and 12.0 g/dL. The US primary efficacy endpoint was the change in Hb from baseline to the mean level during the evaluation period (weeks 29 through 52), regardless of rescue therapy. Hypothesis testing was conducted with a NI margin of -0.75 g/dL as it was for Studies 002, 063, and 064: i.e., NI would be declared if the 95% CI of the difference excluded 0.75 g/dL or more.

The starting dose of roxadustat was based on the previous ESA dose and the protocol provided for adjusting the roxadustat dose to maintain Hb between 10 and 12 g/dL.

Study Patients: Enrolled patients were randomized to roxadustat (n=415) or continued ESA treatment (n=422) for an intended treatment duration of \geq 52 weeks (\leq 104 weeks). Approximately 62% of patients had been using epoetin alfa, and approximately 38% had been using darbepoetin alfa.

Demographics and Baseline Characteristics: The demographics and baseline characteristics were generally well balanced between the two groups. The mean age of patients was approximately 61 years. Most patients were male (58%), White (97%), and on hemodialysis (94%). Mean baseline Hb values were approximately 10.8 g/dL in both groups, and the majority of patients were iron replete at baseline.

Study completion rates were 60% in the roxadustat group and 73% in the ESA group. Deaths occurred in 14.9% of subjects in the roxadustat group vs. 11.2% of subjects in the ESA group.

Table 16: Selected Demographic and Baseline Disease Characteristics—Study 613

	Roxadustat (N=415)	Continued ESA Treatment (N=422)
Age, mean (SD)	61 (13.8)	61.8 (13.4)
Female, n (%)	169 (40.8)	285 (44)
Race, n (%)		
White	405 (97.8)	407 (96.9)
Black	6 (1.4)	6 (1.4)
Asian	1 (0.2)	3 (0.7)
Other	2 (0.5)	4 (1.0)
Hemodialysis, n (%)	379 (91.5)	405 (96.4)
Peritoneal Dialysis, n (%)	35 (8.5)	15 (3.6)
Baseline Hb (g/dL), mean (SD)	10.75 (0.62)	10.77 (0.63)
Diabetes, n (%)	104 (25.1)	133 (31.6)
History of cardiovascular, cerebrovascular, or thromboembolic disease, n (%)	169 (40.8)	201 (47.9)

Efficacy Endpoint

For the primary endpoint of Hb change from baseline averaged over Weeks 28 to 52 regardless of rescue therapy, the study met the noninferiority margin of -0.75 g/dL. The least squares mean difference between roxadustat vs. ESA in the ITT was 0.17 (95% CI: 0.082, 0.26) with p < 0.001 (one-sided).

Safety

Safety is divided into four sections: (1) analyses of adverse events; (2) analyses of laboratory data; (3) analyses of MACE; and (4) explorations of the relationships between thromboembolic events, drug dose, Hb concentration, and rate of change of Hb concentration. In each section, data for the NDD and DD patient populations are presented sequentially. All of these analyses contribute importantly to the assessment of roxadustat's safety.

Studies in the NDD patient population are placebo-controlled. Consequently, they offer the opportunity to assess the safety of roxadustat against a "clean" background. On the other hand, these studies suffer from disparate rates of discontinuation in two treatment groups. As noted above, patients who were doing poorly, some of whom required RBC transfusions, were more likely to discontinue from treatment and discontinue from the study, such they could no longer contribute adverse events. It follows that adverse event rates are dependent on time of observation. Even when adjusted for observation time, the results may be somewhat skewed against roxadustat. Thus, smaller differences in adverse event rates between the roxadustat and placebo groups in the NDD population may be factitious and should be interpreted carefully. (Larger differences, in contrast, merit concern.) In the DD population, studies

were active-controlled (against epoetin alfa) and rates of discontinuation were similar; therefore, interpretation of adverse event rates in this population is straightforward.

Analyses of Adverse Events

Methods

Pooling: Given that the three studies in the NDD population were similar in terms of their patient populations, durations, and Hb targets, simple pooling was used to combine them for the main safety analyses. Of note, however, the randomization ratios differed across the studies (1:1 in study 001, 2:1 in studies 060 and 608), and the studies differed in size, leading to the potential for Simpson's paradox. Nevertheless, we found that the signals that emerged from the pooled analyses were generally consistent across the individual studies.

Definition of "Treatment-emergent": A "treatment emergent" adverse event is defined as an adverse event that was not present prior to treatment but occurs during treatment (or, if present at treatment initiation, an event that worsens in intensity or frequency on-drug). Only treatment-emergent adverse events are considered in this document, as is customary.

Ascertainment Window: When patients are monitored after treatment discontinuation, it is essential to define the "ascertainment window"—the time on-treatment plus the interval of additional monitoring beyond which a causal relationship between the drug and effect would not be reasonably likely. Typical ascertainment windows are the treatment period plus 5 half-lives; however, in many cases, a week or a month are selected—somewhat arbitrarily.

Establishment of the ascertainment window requires careful consideration. For example, alpha1 adrenoreceptor blocking agents would not be expected to cause orthostatic hypotension once they are no longer in the circulation. In contrast, some drugs have the potential to cause long-term sequelae, e.g., pulmonary fibrosis. Thus, it is important to define the ascertainment window, and this is usually done prospectively.

The applicant conducted analyses based on multiple ascertainment windows: on-treatment plus 7 days (OT+7), on-treatment plus 28 days (OT+28), and on-treatment plus all (OT+All), i.e., On-Study. Although longer "windows" have the potential to detect adverse events with longer latency, they also have greater potential for confounding. (For example, some patients initiated other treatments for anemia after discontinuing the study drug that could confound analyses using longer ascertainment windows.) Thus, results for all three "windows" were considered in some of our analyses and are considered complementary. More detail is provided in the section on MACE.

Adverse Event Queries: Study investigators report adverse events using their own language, i.e., 'verbatim terms,' which must be translated into appropriate, standard preferred terms prior to analysis. For example, the verbatim term 'hypotension w/ sepsis from pneumococcus' would be translated to the standard preferred term 'pneumococcal sepsis.'

Verbatim terms can include substantial detail, and disparate but related terms must be combined in order to represent the various safety signals completely and accurately. Thus, the terms 'wound sepsis,' 'neutropenic sepsis,' 'urosepsis,' 'septic shock,' etc. all indicate 'sepsis' and need to be combined. The combination of medically similar and/or related preferred terms for analysis is called a "query." To be

clear, tabulation of individual preferred terms <u>without</u> queries can be highly deceptive. For example, the adverse event term 'sepsis' was reported for 81 patients who received roxadustat in the NDD population, whereas a query for 'sepsis,' including multiple additional adverse events, finds 132 patients. The preferred terms used in some of the more important queries are shown in the appendix.

Standardized MedDRA queries have been available for many years; however, they are not well suited for assessing adverse events in new drug applications. For this reason, FDA is developing a standard set of queries for new drugs. FDA's new queries, as well as other queries developed over many years by FDA staff, were used to assess the adverse events in the roxadustat development program.

Event rate: In the analysis of adverse events, event rates are reported per 100 patient years (P-Y). These calculations include only the incident event (i.e., recurrent events are not counted) and utilize an overall total exposure (dependent upon the ascertainment window applied) across the set of adverse events. In other words, for subjects who experienced an adverse event, follow-up time was not censored after the event in these analyses. For patients who experienced a particular adverse event, the applicant truncated the time of exposure at the time of event (in some analyses). This is a reasonable approach that differs slightly the approach we used; however, the differences in calculated patient exposure are minimal, with essentially no effect on the results.

Drug-relatedness: The most important consideration when assessing adverse events in the consideration of drug safety is relatedness. Merely identifying a risk difference in an adverse event that disfavors a drug does not constitute causality. In our formulation of causality, we considers a drug's mechanism of action, non-clinical (animal) findings, known effects of other drugs in-class, relationship of the adverse event to dose/exposure, consistency of signals in studies across a development program, and consistency across related adverse events (e.g., signals for orthostatic hypotension and falls are self-reinforcing). Finally, consistency between the total numbers of adverse events and serious adverse events can be important, and may play an important role in considering the overall benefit-risk profile.

Results

NDD Patient Population

The NDD patient population included all 4270 randomized subjects who received ≥ 1 dose of study drug in the three major randomized, double-blind, placebo-controlled studies (001, 060, 068). No subjects were on dialysis at the time of randomization, although some initiated dialysis during the study. Some of the adverse events are relatively specific to hemodialysis (e.g., vascular access thrombosis) or peritoneal dialysis (e.g., peritonitis); however, the actual denominators (i.e., numbers of subjects) are unknown. Thus, although the relative risks of such events may be accurate, their absolute risk differences will be underestimated. Analyses are shown separately for Study 610, which employed an active control group instead of a placebo group.

Deaths

Causes of death were adjudicated by an independent event committee and are summarized in Table 17, as reported by the applicant. Their analysis is based on the OT+28 ascertainment window. The "Patients with Events" columns list the numbers of subjects along with the corresponding percentages of patients. As noted above, however, the mean and total time-on-study differed between the roxadustat and placebo groups; therefore, expression of a simple frequency of adverse events (% of patients) is

potentially misleading. The "Events per 100 P-Y" columns (P-Y = patient-year) is corrected for duration of treatment, and provides a more appropriate basis for comparison between the treatment groups. The "Risk Difference" column (red bars) shows the absolute risk difference between the roxadustat and placebo groups, and represents a simple subtraction expressed per 100 P-Y. The "Relative Risk" column (blue bars) is the ratio of the risks (roxadustat/placebo) based on events per 100 P-Y.

Table 17: Adjudicated Causes of Death—Studies 001, 060, 068; Ascertainment Window OT+28

	Patients w	ith events %)	Events (pe	r 100 PY)	Risk	Relative Risk
	Roxadustat	Placebo	Roxadustat	Placebo	Difference	Based on P-Y
	N = 2386	N = 1884	4038 P-Y	2460 P-Y	(per 100 P-Y)	
Total Deaths	260 (10.9)	122 (6.48)	6.44	4.96	1.48	1.30
Cardiovascular-related	105 (4.4)	60 (3.18)	2.60	2.44	0.16	1.07
Sudden cardiac death	48 (2.01)	26 (1.38)	1.19	1.06	0.13	1.12
Acute MI	18 (0.75)	14 (0.74)	0.45	0.57	-0.12	0.78
Stroke	13 (0.54)	8 (0.42)	0.3	0.3	-0.01	0.99
Heart failure	10 (0.42)	10 (0.53)	0.25	0.41	-0.16	0.61
Other cardiovascular	9 (0.38)	2 (0.11)	0.22	0.08	0.14	2.74
Cardiovascular procedure	6 (0.25)	0 (0)	0.15	0.00	0.15	e n e
Non-cardiovascular-related	128 (5.36)	49 (2.6)	3.17	1.99	1.18	1.59
Infection	55 (2.31)	16 (0.85)	1.36	0.65	0.71	2.09
Renal	44 (1.84)	16 (0.85)	1.1	0.7	0.44	1.68
Malignancy	6 (0.25)	2 (0.11)	0.15	0.08	0.07	1.83
Hemorrhage	5 (0.21)	3 (0.16)	0.12	0.12	0.00	1.02
Undetermined	27 (1.13)	13 (0.69)	0.67	0.53	0.14	1.27

Data are compliled from Table 50 in the applicant's Integrated Summary of Safety; P-Y = patient-year

The rate of death was higher in patients who had received roxadustat; the overall risk difference was 1.48 deaths per 100 P-Y, with a relative risk of 1.30. Somewhat fewer than half the deaths were cardiovascular in nature. The leading causes of death (and the largest contributors to the risk difference) were infections, "renal" deaths, and sudden cardiac deaths. Deaths will be discussed in greater detail in the MACE section. The numbers of adjudicated deaths from malignancy are small, but there are more deaths from malignancy in patients who received roxadustat (estimated relative risk = 1.8). Malignancy is of interest because it is a labeled adverse drug reaction for the ESAs.

Deaths in Study 610

In this study of 616 subjects, there were 22 (6.8%) and 18 (6.1%) deaths in the roxadustat and darbepoetin alfa groups, respectively, in the OT+28 analysis. For the On-study analysis, there were 29 (9.0%) and 22 (7.5%) deaths in the respective groups. The numbers of deaths were greater in the roxadustat group, but the difference is too small to be conclusive.

Serious Adverse Events

Table 18 shows the serious adverse events and adverse event queries for the pooled studies in the NDD patient population for the OT+7 ascertainment window. The tabulation (and many that follow in this document) shows a mixture of serious adverse event queries and individual serious adverse event preferred terms, with the later denoted by "term or "actual term." Subjects with more than one serious adverse event for a given preferred term or more than one event within the same query were counted only once.

Adverse events and adverse event queries for which the event rate (per 100 P-Y) is \geq 0.5 with a relative risk \geq 1.3 are shown, along with adverse events of special interest.

Table 18: Serious Adverse Events—Studies 001, 060, and 608; Ascertainment Window OT+7

	Patients with events (%)		Events (per 100 PY)		Risk	
	Roxadustat	Placebo	Roxadustat	Placebo	Difference	Relative Risk Based on P-Y
	N = 2386	N = 1884	3871 P-Y	2323 P-Y	(per 100 P-Y)	
Thromboembolic						
Thrombotic events	140 (5.87)	58 (3.08)	3.62	2.50	1.1	1.45
Device/shunt thrombosis	36 (1.51)	8 (0.42)	0.93	0.34	0.6	2.70
Deep vein thrombosis (term)	20 (0.84)	2 (0.11)	0.52	0.09	0.4	6.00
Myocardial infarction FDA	54 (2.26)	31 (1.65)	1.40	1.33	0.1	1.05
Stroke	53 (2.22)	26 (1.38)	1.37	1.12	0.3	1.22
Ischemic stroke	31 (1.30)	14 (0.74)	0.80	0.60	0.2	1.33
Pulmonary embolism (term)	8 (0.34)	1 (0.05)	0.21	0.04	0.2	4.80
Central Nervous System	_					
Intracranial hemorrhage	24 (1.01)	6 (0.32)	0.62	0.26	0.4	2.40
Seizure FDA	9 (0.38)	1 (0.05)	0.2	0.0	0.2	5.40
Infection	_					
Sepsis/septic shock	87 (3.65)	22 (1.17)	2.25	0.95	1.3	2.37
Urinary tract infection	100 (4.19)	53 (2.81)	2.58	2.28	0.3	1.13
Infection, bacterial	49 (2.05)	17 (0.9)	1.27	0.73	0.5	1.73
Cellulitis	36 (1.51)	13 (0.69)	0.93	0.56	0.4	1.66
Bacteremia	30 (1.26)	10 (0.53)	0.8	0.4	0.4	1.80
Peritonitis	28 (1.17)	10 (0.53)	0.72	0.43	0.3	1.68
Miscellaneous					_	
Acute kidney injury (term)	75 (3.14)	34 (1.8)	1.94	1.46	0.5	1.32
Hyperkalemia (term)	56 (2.35)	22 (1.17)	1.45	0.95	0.5	1.53
Fracture	45 (1.89)	19 (1.01)	1.16	0.82	0.3	1.42
Gastrointestinal hemorrhage	58 (2.43)	29 (1.54)	1.50	1.25	0.3	1.20
Hyponatremia (term)	22 (0.92)	9 (0.48)	0.57	0.39	0.2	1.47
Malignancy FDA	37 (1.55)	23 (1.22)	0.96	0.99	0.0	0.97

Listings labeled "term" represent individual preferred terms.

All other listings represent queries that combine multiple, related adverse event terms.

FDA = FDA query; P-Y = patient-year

Given the problem of differential dropout from the two treatment groups, relative risks less than ~1.3 seem difficult to interpret. The ESAs are known to increase the risk of thrombotic events, and they are listed as adverse drug reactions in their labeling. Roxadustat also shows an obvious signal for serious thrombotic events, with an estimated risk difference (vs. placebo) of 1.1 events per 100 P-Y and a relative risk of 1.45. The largest contributors to the thrombosis query are MI, with 54 events in the roxadustat group, and stroke with 53 events. The numbers of subjects with deep vein thrombosis and pulmonary embolism are relatively small; however, the relative risks are concerning: 6.0 and 4.8, respectively. Importantly, as noted above, the risk difference for device/shunt thrombosis is considerably underestimated, because the analysis assumes that all patients were on dialysis, which is untrue. (Fortunately, additional estimates of the risk of device/shunt thrombosis are available from studies in the DD patient population, shown later, where all subjects are on dialysis and the denominators are certain.)

Seizure is another serious adverse event of special interest, as seizures are an adverse drug reaction with ESAs. Although the numbers of subjects with serious adverse events of seizure are relatively small, the relative risk of 5.4 merits concern (9 vs. 1 event).

The signal of serious infection was unexpected, but sepsis/septic shock is an obvious concern (risk difference 1.3 per 100 P-Y; estimated relative risk = 2.37), and it is reinforced by signals for serious urinary tract infections, bacterial infections, cellulitis, and peritonitis. Again, as noted above, it is safe to assume that most subjects who reported peritonitis were on peritoneal dialysis. Although the relative risk of peritonitis may be reasonably accurate, the risk difference may be underestimated here.

Other notable serious adverse events include acute kidney injury, hyperkalemia, fracture, gastrointestinal hemorrhage, and hyponatremia.

One might reasonably ask whether some serious adverse events were more common in the placebo groups than in the roxadustat groups. Queries for pulmonary edema, anemia, angina, fatigue, hypotension, and dyspnea favored roxadustat, with event rates exceeding 0.5 per 100 P-Y in the placebo groups (≥ 11 events) and relative risks < 0.75.

Study 610

Unlike the placebo-controlled studies above, Study 610 employed darbepoetin alfa as an active comparator, and time-on-treatment was similar between the two groups. Thus, serious adverse events are expressed as simple percentages, without correction for time-on-study. Of note, the total number of subjects in Study 610 was $^{\sim}1/7$ the number of subjects in the three pooled studies.

Table 19 shows serious adverse events (and queries) where the frequency in the roxadustat group was > 5% and the relative risk vs. darbepoetin alfa exceeded ~1.3. Note: the threshold for inclusion of serious adverse events in this table differed from the threshold for the pooled analyses of Studies 001, 060, and 608; however, they correspond to similar numbers of adverse events in roxadustat-treated groups.

¹ The list of adverse event terms in the query is shown in the appendix.

Signals for both serious thrombosis and infection events are again apparent. The thrombosis difference is particularly important because it is evident when compared here to darbepoetin alfa, which is itself known to predispose to thrombotic events.

Table 19: Serious Adverse Events—Study 610

	Roxadustat N = 323	Darbepoetin alfa N = 293	Risk Difference (%)	Relative Risk
N (%)				
Infection, all	48 (14.9%)	34 (11.6%)	3.3	1.28
Bacterial infectious disorders	18 (5.6%)	7 (2.4%)	3.2	2.33
Pneumonia FDA	19 (5.9%)	12 (4.1%)	1.8	1.44
Thrombosis	20 (6.2%)	13 (4.4%)	1.8	1.41

All listing are queries; FDA = FDA query

One might reasonably question whether there were serious adverse events that occurred at a frequency of 5% in the darbepoetin group with a relative risk favoring *roxadustat*. The frequencies for congestive heart failure (query) were 5.0% and 7.5% in subjects treated with roxadustat and darbepoetin alfa, respectively. No other serious adverse events (or queries) were found that favored roxadustat over darbepoetin alfa.

All Adverse Events

Table 20 lists the results of pooled analyses of adverse events and adverse event queries for the three major studies in the NDD patient population, where the event rate was > 2 per 100 P-Y in the roxadustat groups, and the relative risk (vs. placebo) was > 1.2. This listing of \underline{all} adverse events includes the serious adverse events described above.

Table 20 is similar to the previous table, with the addition of estimated relative risks for all ascertainment windows. The heights of the vertical violet bars at right represent the estimated relative risks for the OT+7, OT+28, and OT+All (On-Study) analyses, respectively. Thus, the height of the violet bar at left corresponds to the relative risk for the OT+7 analysis, which matches the relative risk in the column 'Relative Risk Based on P-Y.' The center and right violet vertical bars show the results for the OT+28 and on-study analyses. Inspection of the three violet bars for each listing shows how the risk ratios differ across the ascertainment windows. The relative risks are fairly consistent across the OT+7, OT+28, and On-study ascertainment windows for most of these adverse events. Device/shunt thrombosis/occlusion and sepsis/septic shock are exceptions, where the relative risk decreases somewhat for the OT+All ascertainment window.

Again, there are notable signals for thrombotic events, sepsis/septic shock, bacterial infections, seizures, and hyperkalemia. There is a signal for face edema with a small number of events, but a substantial relative risk (8.4). There are signals for insomnia, rash, peripheral edema, acute kidney injury, and fracture; however, the risk differences are small. Peripheral edema and the query 'edema, fluid retention overload' show risk differences around 1 per 100 P-Y range, and are risks of ESAs. Nausea, vomiting, and dyspepsia all have estimated relative risks of 1.2 with risk differences ~1 per 100 P-Y, and the fact that they were detected together suggests drug-relatedness. Malignancy is neutral.

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Considering the large number of adverse events and queries examined, it is reasonable to consider whether there are signals that favored *placebo*. The only adverse events reported at a rate > 2 per 100 P-Y in patients who received placebo with a relative risk < 0.8 (i.e., worse in the placebo groups) were anemia, asthenia, fatigue, hypotension, and myocardial ischemia.

Table 20: All Adverse Events—Studies 001, 060, and 608; OT+7, OT+28, and OT+All Ascertainment Windows

Adverse Events On-treatment (OT) Plus 7 Days					Relative Risk; On-		
	Patients with events (%)		Events (per 100 P-Y)		Risk Difference	RR Based on	treatment plus 7, 28,
	Rox	Pbo	Rox	Pbo	(per 100 P-Y)	P-Y	99 Days
Numbers of patients -> Patient-years ->	2386	1884	3870	2323) }		
Thombotic Events							
Device/shunt thrombosis, occlusion, malfunction, stenosis #	88 (3.7)	20 (1.1)	2.3	0.9	1.4	2.6	lli
Device/shunt thrombosis (VAT) #	71 (3)	17 (0.9)	1.8	0.7	1.1	2.5	
Thrombosis #	195 (8.2)	76 (4)	5.0	3.3	1.8	1.5	100
Stroke (includes ischemic and hemorrhagic) # Infections	57 (2.4)	29 (1.5)	1.5	1.2	0.2	1.2	III
Sepsis/septic shock #	100 (4.2)	28 (1.5)	2.6	1.2	1.4	2.1	III.
Bacterial infectious disorders HLGT#	207 (8.7)	102 (5.4)	5.3	4.4	1.0	1.2	Ш
Nasopharyngitis FDA N #	129 (5.4)	66 (3.5)	3.3	2.8	0.5	1.2	
Laboratory Abnormalities							
Hyperkalemia #	274 (11.5)	134 (7.1)	7.1	5.8	1.3	1.2	100
Iron deficiency#	114 (4.8)	49 (2.6)	2.9	2.1	0.8	1.4	les.
Gastrointestinal							
Nausea FDA N #	242 (10.1)	117 (6.2)	6.3	5.0	1.2	1.2	100
Dyspepsia FDA N #	155 (6.5)	76 (4)	4.0	3.3	0.7	1.2	
Vomiting FDA N #	148 (6.2)	75 (4)	3.8	3.2	0.6	1.2	
Decreased appetite (actual term)	97 (4.1)	49 (2.6)	2.5	2.1	0.4	1.2	111
Miscellaneous							
Face oedema (actual term)	14 (0.6)	1 (0.1)	0.4	0.0	0.3	8.4	III
Seizure FDA N #	24 (1)	3 (0.2)	0.6	0.1	0.5	4.8	III
Insomnia FDA N #	131 (5.5)	46 (2.4)	3.4	2.0	1.4	1.7	10.
Rash FDA N #	110 (4.6)	53 (2.8)	2.8	2.3	0.6	1.2	***
Oedema peripheral (actual term)	275 (11.5)		7.1	6.0	1.1	1.2	m
Acute kidney injury FDA N #	125 (5.2)	63 (3.3)	3.2	2.7	0.5	1.2	
Fracture #	102 (4.3)	52 (2.8)	2.6	2.2	0.4	1.2	
Edema, fluid retention, overload #	515 (21.6)	289 (15.3)	13.3	12.4	0.9	1.1	101
Systemic hypertension FDA N*	411 (17.2)	224 (11.9)	10.6	9.6	1.0	1.1	***
Malignancy FDA N #	43 (1.8)	34 (1.8)	1.1	1.5	-0.4	0.8	

Listings labeled "actual term" represent individual preferred terms.

[#] All other listings represent queries that combine multiple, related adverse event terms.

[&]quot;FDA N" = FDA query; P-Y = patient-year; RR = relative risk

Study 610

Table 21 shows all adverse events and adverse event queries that were reported at a frequency of > 5% in the roxadustat group, and > 2% higher than in the darbepoetin alfa group in Study 610. (As previously noted, roxadustat was compared to darbepoetin alfa in this study rather than placebo, and time-on-treatment was similar between the two treatment groups.)

Table 21: All Adverse Events—Study 610

	Roxadustat	Darbepoetin alfa	Risk	Relative
	N = 323	N = 293	Difference (%)	Risk
N (%)				
Hyperphosphatemia (term)	23 (7.1%)	9 (3.1%)	4.0	2.29
Edema, fluid retention, overload	62 (19.2%)	45 (15.4%)	3.8	1.25
Peripheral edema FDA	45 (13.9%)	35 (11.9%)	2.0	1.17
Insomnia FDA	18 (5.6%)	6 (2%)	3.6	2.80
Muscle spasms (term)	23 (7.1%)	12 (4.1%)	3.0	1.73
Dyspnea FDA	18 (5.6%)	8 (2.7%)	2.9	2.07
Thrombosis	25 (7.7%)	15 (5.1%)	2.6	1.51
Arrhythmia FDA	38 (11.8%)	28 (9.6%)	2.2	1.23
Nausea (term)	26 (8%)	17 (5.8%)	2.2	1.38
Constipation FDA	19 (5.9%)	11 (3.8%)	2.1	1.55
Headache FDA	18 (5.6%)	10 (3.4%)	2.2	1.65
Hypotension FDA	17 (5.3%)	9 (3.1%)	2.2	1.71
Bronchitis (term)	20 (6.2%)	12 (4.1%)	2.1	1.51

Adverse events denoted by "term" are individual preferred terms. All others are queries. FDA = FDA query

Signals for peripheral edema, edema, fluid retention/overload, insomnia, thrombosis, and nausea have been observed in other studies, and their observation here is reinforcing. In particular, thrombosis and fluid retention/overload are labeled adverse drug reactions for ESAs. Adverse events not heretofore observed include hyperphosphatemia, muscle spasms, dyspnea, arrhythmia, constipation, headache, hypotension, and bronchitis. Analyses of adverse events in the DD patient population will provide a far more robust comparison between roxadustat and darbepoetin alfa.

DD Patient Population

The DD patient population includes 3880 randomized subjects who received ≥ 1 dose of study drug in the three major randomized, double-blind, active-controlled studies (002, 063, 064). Study 063 enrolled subjects who had initiated dialysis within 4 months of randomization. Studies 002 and 064 enrolled such subjects, as well as subjects who had been stable on dialysis and were using an ESA. Subjects were randomized to roxadustat or epoetin alfa. Analyses are shown separately for Study 613, which was conducted in Europe and included randomization to either roxadustat or darbepoetin alfa. Because ESAs were used as active controls for these trials, the adverse event tables include most of the adverse drug reactions currently in the ESA labels.

Deaths

Table 22 provides a tabulation of adjudicated deaths in the DD patient population, with numbers compiled from the applicant's table. There is a slight trend toward a higher rate of death in patients who received roxadustat vs. epoetin alfa. The risk difference was 0.62 deaths per 100 P-Y, with a relative risk of 1.08. Slightly more than half the deaths were cardiovascular in nature. The leading causes of cardiovascular death (and the largest contributors to the risk difference) were acute MI and sudden cardiac death. The leading non-cardiovascular causes of death were infection and "renal" deaths. Deaths will be discussed in greater detail in the MACE section.

Table 22: Adjudicated Causes of Death—Studies 002, 063, 064; Ascertainment Window OT+28

	Patients with events		Events (pe	er 100 PY)		
		(%)			Risk Difference	Relative Risk
	Roxadustat	Epoetin alfa	Roxadustat	Epoetin alfa	(per 100 P-Y)	Based on P-Y
	N = 1940	N = 1940	3447 P-Y	3874 P-Y	(per 100 1-1)	
Total Deaths	282 (14.54)	293 (15.1)	8.18	7.56	0.62	1.08
Cardiovascular-related	159 (8.2)	160 (8.25)	4.61	4.13	0.48	1.12
Sudden cardiac death	86 (4.43)	85 (4.38)	2.50	2.19	0.31	1.14
Acute MI	26 (1.34)	16 (0.82)	0.75	0.41	0.34	1.83
Heart failure	20 (1.03)	17 (0.88)	0.6	0.4	0.14	1.32
Stroke	14 (0.72)	25 (1.29)	0.41	0.65	-0.24	0.63
Other cardiovascular	7 (0.36)	7 (0.36)	0.20	0.18	0.02	1.12
Non-cardiovascular-related	101 (5.21)	102 (5.26)	2.93	2.63	0.30	1.11
Infection	47 (2.42)	46 (2.37)	1.36	1.19	0.17	1.15
Renal	15 (0.77)	10 (0.52)	0.44	0.26	0.18	1.69
Hemorrhage	7 (0.36)	5 (0.26)	0.20	0.13	0.07	1.57
Gastrointestinal	5 (0.26)	10 (0.52)	0.15	0.26	-0.11	0.56
Malignancy	5 (0.26)	7 (0.36)	0.15	0.18	-0.03	08.0
Undetermined	22 (1.13)	31 (1.6)	0.64	0.80	-0.16	0.80

Data are complifed from Table 117 in the applicant's Integrated Summary of Safety; P-Y = patient-year

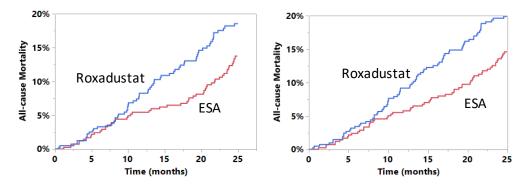
Deaths in Study 613

Study 613 was a European study that randomized stable DD subjects 1:1 to roxadustat (N = 414) or ESA (N = 420). According to the applicant, within the OT+28 ascertainment window, there were 64 (9.7 per 100 P-Y) and 51 (6.8 per 100 P-Y) all-cause deaths in the roxadustat and ESA treatment groups, respectively. The applicant's estimated HR is 1.588 (95% CI 1.096, 2.300); P = 0.015. The risk difference is 2.9 deaths per 100 P-Y.

For the On-study analysis, there were 78 (10.6 per 100 P-Y) vs. 59 (7.4 per 100 P-Y) deaths for the roxadustat and ESA groups, respectively. The applicant's estimated HR was 1.562 (95% CI 1.112, 2.195); p = 0.010. The risk difference is 3.2 deaths per 100 P-Y.

Kaplan-Meier survival curves are shown for the OT+28 and On-study analyses in Figure 4, left, and right. In accord with the applicant's analyses, the log-rank p-values are nominally statistically significant in these unadjusted Kaplan-Meier analyses. Causes of death were not adjudicated, and no predominant causes were apparent based on the preferred terms of adverse events that were cited as leading to death.

Figure 4: Kaplan-Meier Curves for Time to Death—Study 613, OT+28 (left); On-study (right)



Serious Adverse Events

Table 23 shows the serious adverse events and serious adverse event queries for the pooled studies in the DD patient population (OT + 7 ascertainment window). Events and queries are shown for those where the event rate (per 100 P-Y) is \geq 0.5 and the relative risk \geq 1.3, along with adverse drug reactions from the ESA labeling.

Table 23: Serious Adverse Events—Studies 002, 063, and 064; OT+7 Ascertainment Window

	Patients with Events N (%)		Events (per 100 PY)		Absolute ∆ Risk	Relative Risk
	Roxadustat	ESA	Roxadustat	ESA	(per 100 P-Y)	Based on P-Y
	N = 1940	N = 1940	3315 P-Y	3744 P-Y		
Thombotic Events						
Thrombosis	241 (12.42)	201 (10.36)	7.27	5.37	1.90	1.4
Device/shunt thrombosis	121 (6.24)	94 (4.85)	3.65	2.51	1.14	1.5
Deep vein thrombosis (term)	24 (1.24)	7 (0.36)	0.72	0.19	0.53	3.9
Miscellaneous						
Hypoglycemia FDA	29 (1.49)	25 (1.29)	0.87	0.67	0.20	1.3
Gastroenteritis	27 (1.39)	16 (0.82)	0.81	0.43	0.38	1.9
Seizure FDA	26 (1.34)	19 (0.98)	0.78	0.51	0.27	1.6
Pancreatitis FDA	20 (1.03)	11 (0.57)	0.60	0.29	0.31	2.1
Adverse Drug Reactions Known for ESA	As					
Systemic hypertension FDA	89 (4.59)	110 (5.67)	2.68	2.94	-0.26	0.9
Myocardial infarction FDA	88 (4.54)	85 (4.38)	2.65	2.27	0.38	1.2
Infusion site reaction (term)	0 (0)	0 (0)	0.00	0.00	0.00	-
Injection site reaction (term)	0 (0)	0 (0)	0.00	0.00	0.00	-
Bronchospasm FDA	7 (0.36)	4 (0.21)	0.21	0.11	0.10	2.0
Toxic epidermal necrolysis (term)	0 (0)	1 (0.05)	0.00	0.03	-0.03	0.0
Stevens-Johnson syndrome (term)	1 (0.05)	(0)	0.03	0.00	0.03	-
Dyspnea FDA	11 (0.57)	17 (0.88)	0.33	0.45	-0.12	0.7
Peripheral edema FDA	5 (0.26)	2 (0.1)	0.15	0.05	0.10	2.8
Edema, fluid retention/overload	76 (3.92)	76 (3.92)	2.29	2.03	0.26	1.1
Angina	27 (1.39)	30 (1.55)	0.81	0.80	0.01	1.0
Rash FDA	2 (0.1)	2 (0.1)	0.06	0.05	0.01	1.1

All listed adverse events are queries except those denoted by "term," which are individual preferred terms. FDA = FDA query; P-Y = patient-year

Serious thrombotic events and seizures are again prominent. In the NDD patient population, they were detected against a placebo background; importantly, here they are evident even against epoetin alfa, which is itself known to pose these risks. Other signals of concern include serious adverse events of hypoglycemia, gastroenteritis, and pancreatitis.

Many of the adverse drug reactions known for ESAs (Table 23, bottom) are low in frequency and the results are uninterpretable. For the more frequent serious adverse events that are listed as adverse drug reactions for ESAs (e.g., systemic hypertension and edema, fluid retention/overload), event rates with roxadustat are similar to those for epoetin alfa, which would support including them in roxadustat's labeling if the drug is approved. For MI, the relative risk is 1.2. Myocardial infarction will be discussed in detail in the MACE section.

Study 613

Table 24 shows the serious adverse events in that occurred at a frequency > 5% in the roxadustat group with a relative risk (vs. ESAs) that exceeded 1.3. As has been mentioned previously, thrombosis of vascular access is listed as an adverse drug reaction in the ESA labeling (as a warning). The risk of congestive heart failure is also listed as an adverse drug reaction when ESAs are used to target excessive Hb concentrations. Thus, these signals from Study 613 are quite concerning (both with a relative risk of 2 vs. ESAs), because they suggest that roxadustat's risks are even greater than those of ESAs. Moreover, serious bacterial infections were more frequent with roxadustat than with the ESAs, also as noted in studies in the NDD patient population where roxadustat was compared to placebo. Serious adverse events consistent with other adverse drug reactions from the ESA label were infrequent (not shown).

Table 24: Serious Adverse Events—Study 613

N (%)	Roxadustat N = 414	ESA N = 420	Di	Risk fference (%)	Relative Risk
Congestive heart failure	31 (7.5%)	16 (3.8%)	3.7		2.0
Arteriovenous fistula thrombosis (term)	29 (7%)	15 (3.6%)	3.4		2.0
Device/shunt thrombosis	35 (8.5%)	22 (5.2%)	3.3		1.6
Bacterial infectious disorders	23 (5.6%)	16 (3.8%)	1.8		1.5
Thrombosis	52 (12.6%)	43 (10.2%)	2.4		1.2

All listed adverse events are queries except those denoted by "term," which are individual preferred terms.

All Adverse Events

Table 25 lists all adverse events in the three principal studies in the DD patient population where the adverse event rate was > 2 per 100 P-Y and the relative risk (vs. ESAs) exceeded 1.3. The OT+7 ascertainment window was used; however, results were essentially the same when analyzed with the OT+28 and OT+All windows (data not shown). The listings at the bottom of the table show the adverse events that correspond to adverse drug reactions in the ESA labeling.

Roxadustat shows a strong thrombosis signal here, even when compared to epoetin alfa, a drug for which thrombosis is a labeled adverse drug reaction. With 91% of study subjects on hemodialysis, the rates of device/shunt thrombosis (vascular access thrombosis) are approximately 8.2 and 6.1 per 100 P-Y for roxadustat and epoetin alfa, for a risk difference of 2.1 per 100 P-Y and a relative risk of 1.3. Note that this comparison is based on a large number of adverse events: 271 vs. 228 in the roxadustat and epoetin alfa groups, respectively. Deep vein thrombosis is infrequent (29 vs. 19 events), but the relative risk is 1.7. Vomiting appears here and also appears as a risk in the NDD patient population.

Among the adverse events that correspond to adverse drug reactions in the ESA labeling, the signals for rash, malignancy, MI, peripheral edema, and hypertension are most prominent. In fact, all of the adverse events that correspond with the adverse drug reactions of ESAs show relative risks near or above unity (Stevens-Johnson syndrome and toxic epidermal necrolysis excepted; they are rare). Based on these data, the adverse drug reactions in the ESA labeling should convey to the labeling of roxadustat, if approved.

Table 25: All Adverse Events—Studies 002, 063, 064; OT+7 Ascertainment Window

	Events	s, N (%)	Events (pe	r 100 PY)	Risk Difference	Relative Risk
	Roxadustat	Epoetin alfa	Roxadustat	Epoetin alfa	(per 100 P-Y)	Based on P-Y
	N = 1940	N = 1940	3315 P-Y	3744 P-Y	,	
Thombotic Events						
Device/shunt thrombosis/ occlusion/malfunction/stenosis	319 (16.44)	276 (14.23)	9.62	7.37	2.25	1.31
Device/shunt thrombosis	271 (13.97)	228 (11.75)	8.17	6.09	2.08	1.34
Thrombosis	392 (20.21)	344 (17.73)	11.82	9.19	2.63	1.29
Deep vein thrombosis (term) Gastrointestinal	29 (1.49)	19 (0.98)	0.87	0.51	0.36	1.72
Vomiting FDA	161 (8.3)	134 (6.91)	4.86	3.58	1.28	1.36
Gastroenteritis	86 (4.43)	68 (3.51)	2.59	1.82	0.77	1.43
Miscellaneous					_	
Headache FDA	198 (10.21)	157 (8.09)	5.97	4.19	1.78	1.42
Hypotension FDA	230 (11.86)	199 (10.26)	6.94	5.32	1.62	1.31
Fatigue FDA	115 (5.93)	97 (5)	3.47	2.59	0.88	1.34
Pruritus FDA	103 (5.31)	85 (4.38)	3.11	2.27	0.84	1.37
Muscle spasms (term)	107 (5.52)	92 (4.74)	3.23	2.46	0.77	1.31
Hypoglycemia FDA	79 (4.07)	70 (3.61)	2.38	1.87	0.51	1.27
Tachycardia FDA	73 (3.76)	60 (3.09)	2.20	1.60	0.60	1.37
Adverse Drug Reactions Known for ES	<u>As</u>					
Systemic hypertension FDA	365 (18.81)	367 (18.92)	11.01	9.80	1.21	1.12
Edema, fluid retention, overload	234 (12.06)	260 (13.4)	7.06	6.95	0.11	1.02
Dyspnea FDA	129 (6.65)	150 (7.73)	3.89	4.01	-0.12	0.97
Peripheral edema FDA	98 (5.05)	95 (4.9)	2.96	2.54	0.42	1.16
Myocardial infarction FDA	91 (4.69)	87 (4.48)	2.74	2.32	0.42	1.18
Rash FDA	67 (3.45)	53 (2.73)	2.02	1.42	0.60	1.43
Angina	50 (2.58)	76 (3.92)	1.51	2.03	-0.52	0.74
Bronchos pas m FDA	13 (0.67)	18 (0.93)	0.39	0.48	-0.09	0.82
Angioedema FDA	4 (0.21)	5 (0.26)	0.12	0.13	-0.01	0.90
Anaphylactic reaction FDA	3 (0.15)	4 (0.21)	0.09	0.11	-0.02	0.85
Injection site reaction	2 (0.1)	2 (0.1)	0.06	0.05	0.01	1.13
Infusion site reaction, reaction	1 (0.05)	7 (0.36)	0.03	0.19	-0.16	0.16
Stevens-Johnson syndrome (term)	1 (0.05)	0 (0)	0.03	0.00	0.03	-
Toxic epidermal necrolysis (term)	0 (0)	1 (0.05)	0.00	0.03	-0.03	0.00
Malignancy FDA	38 (1.96)	36 (1.86)	1.15	0.96	0.19	1.19
Seizure FDA	45 (2.32)	33 (1.7)	1.36	0.88	0.48	1.54

Adverse events denoted by "term" are individual preferred terms. All others are queries.

Study 613

Table 26 shows the adverse events in that occurred at a frequency > 5% in the roxadustat group with a relative risk (vs. ESAs) that exceeded 1.3, as well as other significant adverse events. The thrombotic adverse events are once again prominent, even against the background of ESAs. (Of note, there are only a few strokes and MIs, and these favor the roxadustat group over the ESA group.) Signals for nausea and congestive heart failure are also obvious, and have been observed in other trials. With respect to the adverse events that correspond to adverse drug reactions in the ESA labels, the only adverse event with a significant number of events is systemic hypertension, which slightly favors roxadustat vs. ESAs.

Table 26: All Adverse Events—Study 613

N (%)	Roxadustat N = 414	ESA N = 420	Risk Difference (%)	Relative Risk
Thrombotic Events				
Thrombosis	77 (18.6%)	65 (15.5%)	3.10	1.2
Deep vein thrombosis (term)	6 (1.4%)	0 (0%)	1.40	-
Pulmonary embolism (term)	4 (1%)	2 (0.5%)	0.50	2.0
Device/shunt thrombosis	64 (15.5%)	45 (10.7%)	4.80	1.4
Arteriovenous fistula thrombosis (term)	50 (12.1%)	31 (7.4%)	4.70	1.6
Myocardial infarction FDA	10 (2.4%)	17 (4%)	-1.60	0.6
Ischemic stroke	1 (0.2%)	6 (1.4%)	-1.20	0.2
Miscellaneous				
AV fistula thrombosis/occlusion/ malfunction/stenosis	71 (17.1%)	57 (13.6%)	3.50	1.3
Nausea FDA	30 (7.2%)	8 (1.9%)	5.30	3.8
Congestive heart failure	34 (8.2%)	20 (4.8%)	3.40	1.7
Pruritus FDA	25 (6%)	12 (2.9%)	3.10	2.1
Dizziness FDA	25 (6%)	17 (4%)	2.00	1.5
Adverse Drug Reactions Known for ESAs			0.00	-
Systemic hypertension FDA	79 (19.1%)	85 (20.2%)	-1.10	0.9
Edema, fluid retention, overload	18 (4.3%)	23 (5.5%)	-1.20	0.8
Dyspnea FDA	16 (3.9%)	15 (3.6%)	0.30	1.1
Myocardial infarction FDA	10 (2.4%)	17 (4%)	-1.60	0.6
Peripheral edema FDA	10 (2.4%)	9 (2.1%)	0.30	1.1
Rash FDA	9 (2.2%)	11 (2.6%)	-0.40	0.8
Angina	8 (1.9%)	12 (2.9%)	-1.00	0.7
Bronchospasm FDA	1 (0.2%)	1 (0.2%)	0.00	1.0
Toxic epidermal necrolysis	1 (0.2%)	0 (0%)	0.20	-
Infusion site reaction	0 (0%)	0 (0%)	0.00	-
Injection site reaction	0 (0%)	0 (0%)	0.00	-
Stevens-Johnson syndrome	0 (0%)	0 (0%)	0.00	-

All listed adverse events are queries except those denoted by "term," which are individual preferred terms. FDA = FDA query

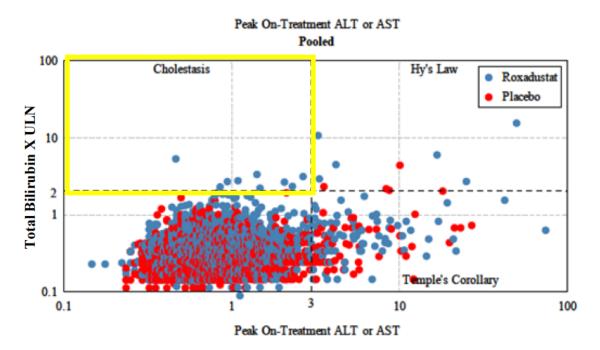
Laboratory Findings

Laboratory findings were analyzed separately for the NDD and DD patient populations. The only important finding was related to abnormal hepatic laboratory values. We obtained expert consultation from the Division of Hepatology and Nutrition, who conferred with the Office of Surveillance and Epidemiology.

NDD population

Figure 5 is a standard eDISH scatterplot of total bilirubin (x upper limit of normal [ULN]) by peak alanine aminotransferase (ALT) or aspartate aminotransferase (AST) (x ULN) for the three principal studies in the NDD population. There were nine cases of increased total and direct bilirubinemia in the roxadustat treatment arms, vs. none in placebo (left upper cholestasis quadrant, yellow highlighted area). Few appeared in the right upper quadrant of the cholestatic scatterplot (data not shown), indicating that most of these jaundiced, cholestatic cases did not have significant elevations in alkaline phosphatase (AP). There was also a modest overall shift in patients in the roxadustat arm toward the upper right part of the eDISH plot (higher ALT/AST, higher bilirubin).

Figure 5: NDD population—Plot of Hepatocellular Injury (Total Bilirubin vs. ALT or AST)



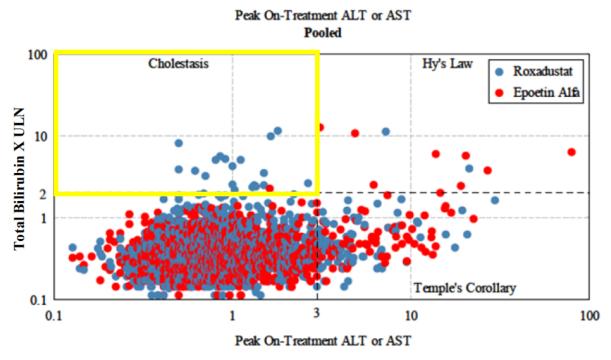
DD population

The eDISH scatterplot (Figure 6) does not show the same general shift in roxadustat-treated patients toward the upper right quadrant as was observed in the NDD trials. With equal randomization to roxadustat or epoetin alfa, there tend to be fewer roxadustat-treated patients in the Hy's Law and Temple's Corollary quadrants.

As was observed in the NDD studies, however, in the left upper cholestasis quadrant (yellow highlighted area) there are 19 roxadustat-treated subjects vs. 1 in epoetin alfa-treated subject. Few subjects

appeared in the right upper quadrant of the cholestatic scatterplot (data not shown). These findings also suggest direct hyperbilirubinemia, not accompanied by significant AP elevations.

Figure 6: DD population—Plot of Hepatocellular Injury (Total Bilirubin vs. ALT or AST)



For both the NDD and DD patient populations, our experts reviewed narratives and clinical details on all patients with important abnormalities in liver tests, and found a total of 19 patients of potential concern for severe DILI with jaundice, either cholestatic, hepatocellular, or mixed pattern. They assessed all cases as unlikely to represent liver injury due to roxadustat. All had a more likely competing diagnosis (e.g., sepsis, gallstone disease, shock liver, congestive hepatopathy, acute viral hepatitis), latency inconsistent with DILI, or resolution despite continuation of drug and/or negative re-challenge.

In summary, roxadustat may cause bland cholestasis (elevated bilirubin without significant elevation in hepatic transaminases), but no significant hepatocellular injury. For the overall NDD and DD populations, there were 19 cases in 4326 roxadustat-treated subjects, i.e., a rate of 0.44%. There were no Hy's Law cases; indeed, careful analysis of all suspicious cases revealed no cases of obvious DILI.

Bland cholestasis generally carries a good prognosis if the inciting event is resolved or the drug is held. Examples of drugs that cause DILI-related bland cholestasis include estrogens and androgens. The recommendation from our consultants was that bland cholestasis would not merit a Warning in labeling; however, for elevations of bilirubin/AP, the drug should be held until resolution, absent clear evidence of another cause, e.g., sepsis.

Analysis of MACE

NDD Patient Population

The objective of the NDD MACE assessment was to demonstrate non-inferiority of roxadustat compared with placebo with respect to cardiovascular risk, based on a meta-analysis of the three principal phase 3

randomized, placebo-controlled trials (001, 060, 608). As noted above, MACE was a composite endpoint that included MI, stroke, and all-cause mortality. Study endpoints were adjudicated by an independent clinical endpoint committee, whose members were blinded to treatment assignment.

The FDA did not agree prospectively on a risk margin and did not agree on the interpretation of the results using strictly a non-inferiority hypothesis testing approach. As such, our interpretation focuses on the estimation of the MACE risk and the uncertainty around it (95% confidence interval) in the NDD patient population.

The MACE meta-analysis included pre-specified, trial-specific stratification factors. The applicant also provided results using common stratification factors defined post hoc. The findings were qualitatively similar, regardless of the stratification factors.

Event Ascertainment Window: The ascertainment window for the primary analysis included the entire study duration, regardless of treatment exposure after randomization, referred to as the On-study analysis. An analysis using the OT+7 ascertainment window was conducted as a sensitivity analysis.

Analysis Model: For each trial, Cox regression was used to model the treatment effect (roxadustat vs. placebo), stratified by baseline Hb values ($< 8 \, \text{g/dL} \, \text{vs.} \ge 8 \, \text{g/dL}$); history of cardiovascular, cerebrovascular, or thromboembolic diseases (yes vs. no); baseline eGFR ($< 30 \, \text{vs.} \ge 30$); and geographic region (US vs. others for Studies 001 and 608; Western Europe vs. others for Study 608). Hazard ratios from each trial were combined using weights inversely proportional to the variance of the study-specific log HR estimates, thereby providing an overall estimate of the HR and its uncertainty (95% CI). This approach preserves the randomization of each trial and avoids a naïve assumption that the patient samples in each trial are exchangeable.

MACE Composite Endpoint—NDD Population: Results for time to first MACE for both the on-study and OT+7 analyses are shown in Table 27.

Table 27: Summary of MACE Anal	ysis Results in the NDD Population
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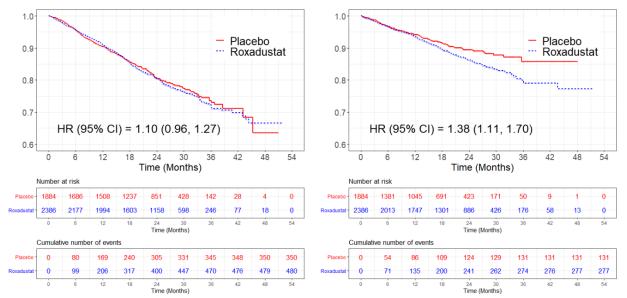
	On-study Analysis (Primary)			OT+7 Analysis (Sensitivity)				
	Roxadustat Placebo			Roxadustat	Placebo			
	N = 2386 N = 1884 PY = 4509.6 PY = 3406.2			N = 2386	N = 1884			
				PY = 3843.2	PY = 2331.6			
Events (rate)	480 (10.6)	350 (10.3)		277 (7.2)	131 (5.6)			
HR (95% CI)	1.10 (0.96, 1.27)			1.38 (1.11, 1.70)				

There is a considerable difference between the estimated HRs for the primary On-study analysis and the OT+7 sensitivity analyses, with HRs (95% CI) of 1.10 (0.96, 1.27) and 1.38 (1.11, 1.70), respectively. Whereas the results seem reassuring for the On-study analysis, the lower limit of the 95% CI for the OT+7 sensitivity analysis (1.11) excludes 1.0. Although the exclusion of 1 in the OT+7 analysis merits concern, the differential exposure between roxadustat and placebo complicates the interpretation of the OT+7 analysis in isolation, as this may not represent a fair randomized comparison. For example, subjects who discontinue treatment early (higher in placebo than roxadustat) are censored at the point of treatment discontinuation. In a population in which MACE occurs at a rate > 5 per 100 PY, because subjects in the roxadustat arm are exposed to treatment for a longer duration, they are at risk for a

longer period of time. Thus, the differential dropout may contribute to a biased estimate of the treatment effect in the OT+7 analysis that disfavors roxadustat.

Figure 7 shows the Kaplan-Meier survival curves for MACE. Of note, the OT+7 analysis includes ~22% less follow-up time than the On-study analysis. Event rates (roxadustat vs. placebo) were 10.6 and 10.3 per 100 P-Y in the On-Study analysis, and 7.2 and 5.6 per 100 P-Y in the OT+7 analysis. Many events occurred beyond the 7-day post-treatment window of the OT+7 analysis, with disproportionately more events in the placebo group, especially for all-cause death.

Figure 7: Time to First MACE— On-study Analysis (Left); OT+7 Analysis (Right)



Source: FDA analysis.

MACE results are shown graphically by study, as well as by its components, for the On-study analysis (Figure 8) and the OT+7 analysis (Figure 9). For the On-study analysis where the overall estimated HR for MACE is 1.10, there are trends for increased stroke, and particularly increased MI, in the roxadustat treatment groups (Figure 8). For the OT+7 analysis where the overall estimated HR for MACE is 1.38, there is a nominally statistically significant finding for all-cause mortality (not favoring roxadustat), which is driven by the Study 001, the largest study (Figure 9). There are also trends for higher rates of stroke and MI for roxadustat, and these trends are fairly consistent across the three studies.

² Note that for this composite endpoint, the sums of the individual component events do not equal the total numbers of first MACE.

Figure 8: MACE and its Components for Studies in the NDD Population (On-study Analysis)

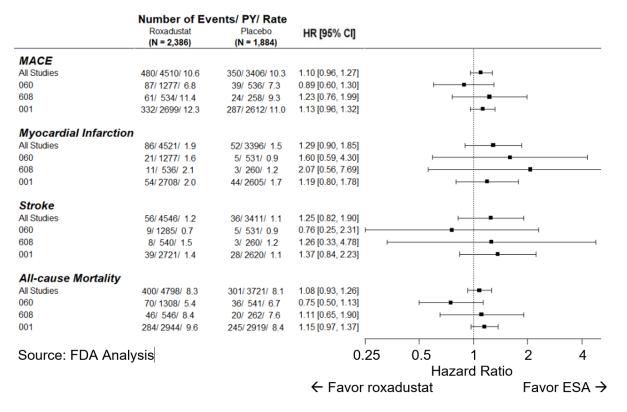


Figure 9: MACE and its Components for Studies in the NDD Population (OT+7 Analysis)

	Roxadustat	ents/ PY/ Rate Placebo	HR [95% CI]		
	(N = 2,386)	(N = 1,884)	1 1987 1 1 1 1 1 1 1 1		
MACE					
All Studies	277/ 3843/ 7.2	131/2332/5.6	1.38 [1.11, 1.70]	⊢ ■	
060	40/ 1124/ 3.6	11/ 382/ 2.9	1.19 [0.60, 2.35]	⊢	
608	40/ 470/ 8.5	18/ 201/ 9.0	0.89 [0.50, 1.59]	- ■	
001	197/ 2249/ 8.8	102/ 1749/ 5.8	1.51 [1.19, 1.92]	⊢ ■	
Myocardial Infarction	,				
All Studies	72/3869/ 1.9	37/2340/ 1.6	1.22 [0.81, 1.84]	⊢	
060	18/ 1133/ 1.6	4/ 382/ 1.0	1.49 [0.50, 4.46]		
608	11/ 473/ 2.3	3/ 201/ 1.5	1.41 [0.37, 5.44]	-	—
001	43/2264/ 1.9	30/ 1757/ 1.7	1.16 [0.72, 1.85]	—	
Stroke					
All Studies	48/3888/ 1.2	21/2350/ 0.9	1.53 [0.91, 2.57]		
060	9/ 1138/ 0.8	2/ 383/ 0.5	1.88 [0.40, 8.82]	-	
608	6/ 477/ 1.3	3/ 202/ 1.5	0.83 [0.20, 3.41]		
001	33/ 2273/ 1.5	16/ 1765/ 0.9	1.65 [0.91, 3.01]	-	
All-cause Mortality					
All Studies	183/3914/4.7	85/2358/ 3.6	1.40 [1.08, 1.82]	⊢	
060	18/ 1146/ 1.6	6/ 383/ 1.6	0.82 [0.32, 2.14] ⊢		
608	24/ 480/ 5.0	14/ 202/ 6.9	0.72 [0.36, 1.42]		
001	141/ 2287/ 6.2	65/ 1773/ 3.7	1.68 [1.25, 2.26]		
	1411 22011 0.2	03/17/3/ 3.1	1.00 [1.20, 2.20]		
			0.25	0.5 1 2 4	
	. 1		0.25	0.5 1 2 4	
Source: FDA analysis			Hazard Ratio		
·	,		← Favor roxa	adustat Favor ESA	\rightarrow

MACE in Study 610

Study 610 compared roxadustat to darbepoetin alfa, rather than a placebo. Results for time to first MACE are shown in Table 28 for the On-study and OT+7 approaches. For both analyses, the estimated HRs tended to favor roxadustat over darbepoetin alfa; however, the results were not statistically significant.

Table 28: Summary of MACE Results in Study 610

	On-study Analysis			OT+7 Analysis			
	Roxadustat N = 323	Darbepoetin alfa N = 293		Roxadustat N = 323	Darbepoetin alfa N = 293 PY = 477.1		
	PY = 575.7 PY = 522.6			PY = 517.7			
Events (rate per 100 P-Y)	49 (8.5)	48 (9.2)		31 (6.0)	39 (8.2)		
HR (95% CI)	0.89 (0.60, 1.33)			0.70 (0.44, 1.12)			

PY = patient years; OT+7 = On-treatment + 7 days analysis

DD Patient Population:

The objective of the MACE assessment in the DD population was to demonstrate non-inferiority of roxadustat to ESA, based on a meta-analysis of the three principal, phase 3, randomized, ESA-controlled trials (002, 063, 064). MACE was defined as it was for the NDD Population: the composite of all-cause mortality, MI, and stroke, and study endpoints were adjudicated by a blinded, independent clinical endpoint committee. The FDA did not agree prospectively on a risk margin using strictly a non-inferiority hypothesis testing approach. As such, our interpretation focuses on the estimation of the MACE risk and the uncertainty around it (95% CI) in the DD patient population. The primary analysis of MACE was based on the meta-analysis using pre-specified, trial-specific stratification factors.

Event Ascertainment Window: Two ascertainment windows were pre-specified in the protocol. The window of event ascertainment for the primary analysis was to include MACE that occurred after the first dose date and within 7 days after the last dose of study drug, or until the first dose of another anemia drug other than the randomized treatment. This is referred to as the OT+7 analysis.

As a sensitivity analysis, an On-study analysis was conducted that included events occurring during the study regardless of the treatment exposure after randomization.

Analysis Model: For each trial, Cox regression was used to model the treatment effect (roxadustat vs. ESA), stratified by geographic region (US vs. non-US); history of cardiovascular, cerebrovascular, or thromboembolic diseases (yes vs. no); screening Hb values (\leq 8 g/dL vs. > 8 g/dL for Study 063; \leq 10.5 g/dL vs. > 10.5 g/dL for Studies 064 and 002); average prescribed weekly ESA dose in the 4 weeks prior to randomization (epoetin alfa dose, or equivalent epoetin alfa dose for patients on non-epoetin alfa ESA at baseline, of \leq 150 vs. > 150 IU/kg/week for Study 064; not included as a stratification variable for Studies 063 and 002); and incident vs. stable dialysis (dialysis duration \leq 4 months vs. > 4 months for Study 002; not included as stratification variable for Studies 063 and 064). HRs were estimated for each study and then combined using weights inversely proportional to the variance of the study-specific log HR estimates to provide an overall estimate of the HR and its uncertainty (95% CI).

On-treatment Analysis Result (Primary Analysis): Comparing roxadustat to epoetin alfa, the estimated HR (95% CI) for time to first MACE event was 1.02 (0.88, 1.20), i.e., neutral (Table 29). There were 306

and 339 subjects with MACE in the roxadustat and ESA groups, respectively, with follow-up time-adjusted incidence rates of 9.4 and 9.3 per 100 P-Y.

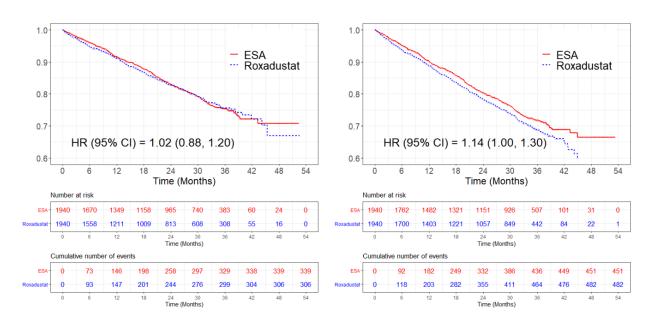
On-study Analysis Result (Sensitivity Analysis): The estimated HR (95% CI) for time to first MACE event was 1.14 (1.00, 1.30), such that the difference was nearly statistically significant (Table 29). There were 482 and 451 subjects with MACE in the roxadustat and ESA groups, respectively, with follow-up time-adjusted incidence rates of 12.4 and 10.9 per 100 P-Y. The HR was driven by differences in all-cause mortality and MI; stroke was neutral.

Table 29: Summary of MACE Analysis Results in the DD Population

	OT+7 Analysis (Primary)			On-Study Analysis (Sensitivity)		
	Roxadustat ESA			Roxadustat	ESA	
	N = 1940	N = 1940		N = 1940	N = 1940	
	PY = 3261.2	PY = 3660.3		PY = 3898.9	PY = 4151.0	
Events (rate per 100 P-Y)	306 (9.4)	339 (9.3)		482 (12.4)	451 (10.9)	
HR (95% CI)	1.02 (0.88, 1.20)			1.14 (1.00, 1.30)		

Kaplan-Meier plots for time to first MACE are shown for the OT+7 and On-study analyses in Figure 10.

Figure 10: Time to First MACE—OT+7 Analysis (Left); On-study Analysis (Right)



Source: FDA analysis.

Figure 11 and Figure 12 show the results by MACE component and by study for the OT+7 and On-study analyses, respectively. ³ The study-specific estimates and confidence intervals are illustrated for comparison.

³ Note that for this composite endpoint, the sums of the individual component events do not equal the total numbers of first MACE.

Figure 11: MACE and its Components for Studies in the DD Population (OT+7 Analysis)

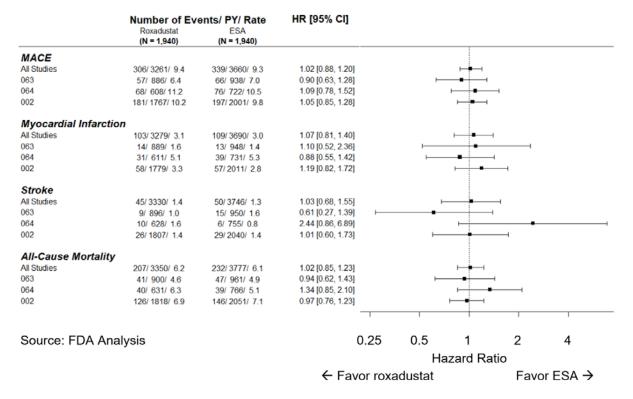


Figure 12: MACE and its Components for Studies in the DD Population (On-Study Analysis)

	Number of Events/ PY/ FAIR		HR [95% CI]					
	Roxadustat (N = 1,940)	ESA (N = 1,940)						
MACE								
All Studies	482/3898.9/12.4	451/4151.0/10.9	1.14 [1.00, 1.30]			⊢= ⊣		
063	85/ 1004.5/ 8.5	82/1048.7/7.8	1.07 [0.79, 1.45]			⊢	4	
064	112/ 725.2/ 15.4	102/ 824.1/12.4	1.24 [0.94, 1.62]			+		
002	285/ 2169.2/ 13.1	267/ 2278.1/ 11.7	1.13 [0.95, 1.33]			+		
Myocardial Infarction	on							
All Studies	124/3917.5/ 3.2	115/4174.1/ 2.8	1.14 [0.88, 1.47]			H-	4	
063	17/ 1010.7/ 1.7	14/ 1061.5/ 1.3	1.24 [0.61, 2.51]		-			ı
064	37/ 732.1/ 5.1	41/ 832.2/ 4.9	0.95 [0.61, 1.49]		-		-	
002	70/ 2174.7/ 3.2	60/ 2280.4/ 2.6	1.24 [0.88, 1.75]			-		
Stroke								
All Studies	58/3986.3/ 1.5	60/4235.6/ 1.4	1.04 [0.72, 1.50]		1		-	
063	11/1016.7/ 1.1	15/ 1061.4/ 1.4	0.74 [0.34, 1.61]			• •	-1	
064	13/ 752.3/ 1.7	8/ 860.0/ 0.9	2.01 [0.82, 4.92]			-	-	
002	34/ 2217.3/ 1.5	37/2314.2/ 1.6	0.98 [0.61, 1.56]		-	-	-	
All-Cause Mortality	,							
All Studies	413/4178.7/ 9.9	369/4396.3/8.4	1.17 [1.02, 1.35]			H=		
063	74/ 1025.2/ 7.2	66/ 1075.7/ 6.1	1.19 [0.85, 1.66]					
064	92/ 767.5/ 12.0	72/ 874.8/ 8.2	1.43 [1.05, 1.96]			⊢		
002	247/ 2386.1/ 10.4	231/2445.8/ 9.4	1.09 [0.91, 1.31]			H-		
			1			1	1	1
			0.25	0.	.5	1	2	4
Source: FDA	analysis				Ha	azard Ra	tio	
	•		← Favor	roxadu	stat		F	avor ESA -
			\ Tavor	CAGGG	Juli		1 6	AVOI LOA

Adjudicated Death: During the OT+7 period in the combined DD studies, there were 207 and 232 deaths in roxadustat and epoetin alfa treated subjects, respectively, with exposure-adjusted rates of 6.2 and 6.1 per 100 P-Y. The estimated HR was 1.02 (0.84, 1.23) (Figure 11).

In the On-Study analysis, the HR was 1.17, with a 95% CI that excluded 1 (1.02, 1.35) (Figure 12). There were 413 and 369 deaths in roxadustat and epoetin alfa treated subjects, respectively, with exposureadjusted rates of 9.9 and 8.4 per 100 P-Y. The estimated HRs for all-cause mortality were fairly consistent across the 4 studies, and ranging from 1.09 to 1.43.

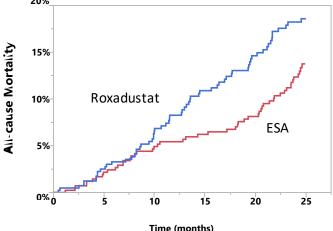
Study 613

Study 613 was not part of the pooled analysis because of differences in study design, however, there were 57 deaths (8.9 per 100 PY) in roxadustat-treated patients (N = 414) vs. 45 (6.3 per 100 PY) in the ESA group (N = 420) in the OT+7 ascertainment window. The nominal HR was 1.54, and the 95% CI (1.04, 2.28) excluded 1. There were additional deaths in the OT+28 and On-study analyses; however, the estimated HRs were similar and the 95% CIs also excluded 1.

Figure 13 shows the Kaplan-Meier graph for all-cause mortality for Study 613, OT+28 ascertainment window.



Figure 13: All-cause Mortality—Study 613; OT+28 Ascertainment Window



Relation Between Thrombotic Events, Roxadustat Dose, Hb Level, and **Hb Rate of Change**

The relation between the risk of adverse cardiovascular events, ESA dose, Hb concentration, and Hb rate of change has been of longstanding interest to FDA. The issues were initially raised in FDA's 2001 review of the Biologics License Application for darbepoetin alfa [10]. Given the similar nature of the safety signals for darbepoetin alfa and roxadustat and questions about roxadustat dose and excursions in Hb, we performed similar analyses for thromboembolic adverse events for the key studies in the roxadustat application, and asked the applicant to conduct the analyses to corroborate our findings.

Analyses were conducted for the OT+7 ascertainment window, separately for the NDD and DD populations. Only the first thromboembolic event was considered for patients who experienced more than one event.

Thromboembolic Events in Relation to Drug Dose

- A. The mean study drug dose (adjusted for weight) was calculated for each subject, and subjects were arranged in quintiles on this basis (by treatment group). The numbers of thromboembolic events were tabulated by dose quintile for both treatment groups and expressed as percent of subjects with events.
- B. Because these drugs are titrated to effect throughout the treatment period, an alternative analysis was conducted using a moving average of the dose. Specifically, for each week on treatment, the mean weight-adjusted dose was calculated for the preceding 4 weeks. For example, the dose at Week 16 was the mean dose during Weeks 12 through 16. Based on the mean weight-adjusted dose for each week, the patient-weeks were divided into quintiles, and the numbers of thromboembolic events were tabulated by quintile for both treatment groups. Event rates were expressed as events per 52 patient-weeks (P-Y). A similar analysis was conducted on the basis of the weight-adjusted dose during 2-week intervals preceding the events. Finally, the analysis was conducted on the basis of the weight-adjusted dose most proximal to the event (previous week).

NDD Patient Population

The relation between overall weight-adjusted study agent dose and thromboembolic events is shown in Figure 14 for the NDD subject population. The figure shows the 5 quintiles from lowest (Q1) to highest (Q5) dose. The y-axis shows the percent of subjects with events, and the numbers in each bar represent the numbers of subjects with events. There appear to be fewer events in Q1, the quintile with the lowest overall weight-adjusted dose.

Figure 14: Thromboembolic Events vs. Overall Total Weight-adjusted Dose of Study Agent—NDD Population

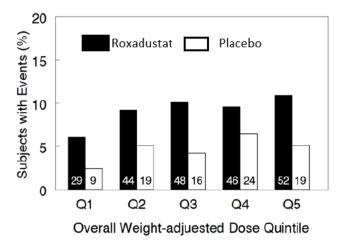
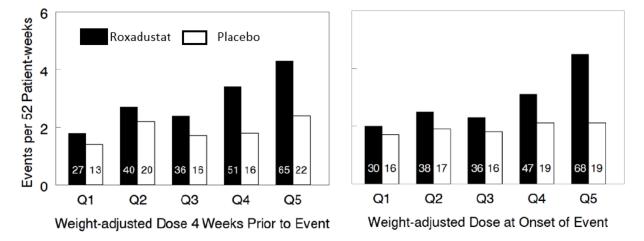


Figure 15 shows the relation between the rate of thromboembolic events (per 52 patient-weeks) and the weight-adjusted doses administered in the 4 weeks preceding the event (left) and the week preceding the event (right). The numbers inside the bars represent the numbers of events. Here, there are fairly strong associations between the preceding dose and thromboembolic events in roxadustat-

treated subjects. As expected, no association is evident in subjects who received placebo. The results for the 2 analyses are similar.

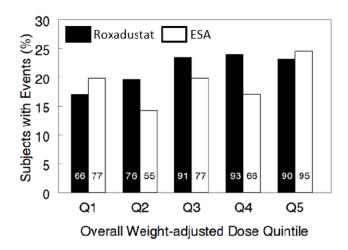
Figure 15: Thromboembolic Events vs. Weight-adjusted Dose of Study Agent—Received in Preceding 4 Weeks (Left); Received at Onset of Event (Right)—NDD Population



DD Patient Population

Figure 16 shows relations between weight-adjusted study agent dose and thromboembolic events. There appears to be a weak association between total dose and probability of a thromboembolic event in roxadustat-treated subjects. For subjects who received ESAs, there is no clear association.

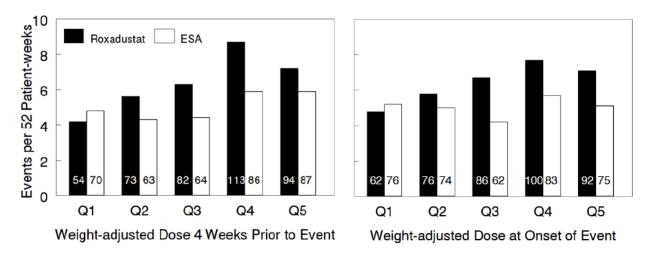
Figure 16: Thromboembolic Events vs. Overall Total Weight-adjusted Dose of Study Agent—DD Population



For subjects who received ESAs, the association is not clear. The results for the two analyses are similar.

Figure 17 shows a reasonable association between weight-adjusted dose and the rate of thromboembolic events in subjects who received roxadustat. For subjects who received ESAs, the association is not clear. The results for the two analyses are similar.

Figure 17: Thromboembolic Events vs. Weight-adjusted Dose of Study Agent—Received in Preceding 4 weeks (Left); Received at Onset of Event (Right)—DD Population



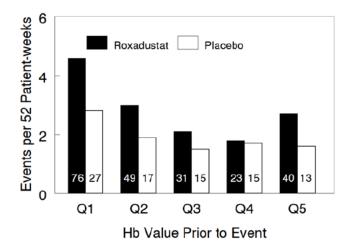
Thromboembolic Events in Relation to Hb Concentration

Hb values were estimated for all subjects for all weeks on-treatment, and the patient-weeks were placed into quintiles on this basis, separately by treatment arm. The numbers of thromboembolic events were assessed for each quintile for both treatment arms and expressed as rate per 52 patient-weeks.

NDD Patient Population

Figure 18 shows the relation between the rate of thromboembolic events and Hb concentration. It has been observed in a number of Hb target studies that subjects with lower Hb values are at higher risk of cardiovascular events. Thus, the relation seen in the figure is not surprising, although the increase in events in the highest quintile (Q5) in roxadustat-treated subjects suggests that targeting higher Hb values may lead to excess thromboembolic events.

Figure 18: Thromboembolic Events vs. Hb at the Time of Event—NDD Population

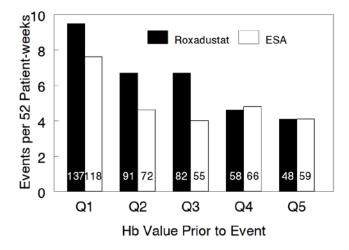


DD Patient Population

Figure 19 shows the relation between the rate of thromboembolic events and Hb concentration in the DD population, and once again there are greater numbers of cardiovascular events with lower Hb

values. The greater event rate in Q5 in the roxadustat subjects is not observed here as is was in the NDD population.

Figure 19: Thromboembolic Events vs. Hb at the Time of Event—DD Population



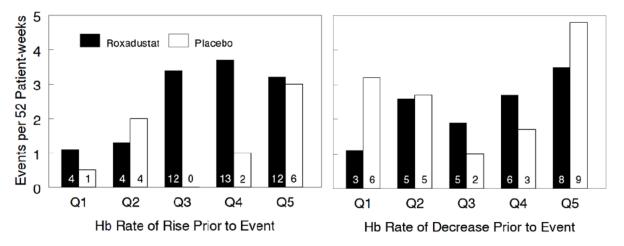
Thromboembolic Events in Relation to Hb Rate of Change

The Hb rate of change (g/dL/week) was estimated for each week that each subject was on treatment by fitting a linear regression line through the Hb values obtained during the preceding 4 weeks. Patientweeks with a rising Hb level (Hb vs. time slope was ≥ 0) were placed in quintiles. The adverse events were tabulated for each quintile for both treatment arms, and results were expressed as adverse events per 52 patient-weeks (P-Y). A similar analysis was conducted for Hb rate of decline, based on patientweeks with a falling Hb level (Hb vs. time slope < 0). Of note, rates of rise and decline could be estimated for only a limited number of events because Hb assessments were scheduled less frequently later in the trials, and two values were necessary to calculate a slope. The majority of the thromboembolic events occurred when only one Hb assessment was available and rate of change could not be estimated.

NDD Patient Population

Figure 20 shows the relation between thromboembolic events an Hb rate of rise leading up to the event. The numbers of events are quite small; most events did not have two Hb values leading up to the event that were necessary to calculate a slope. Nevertheless, there appears to be an association suggesting that limiting Hb rate of rise could decrease the incidence of thromboembolic events.

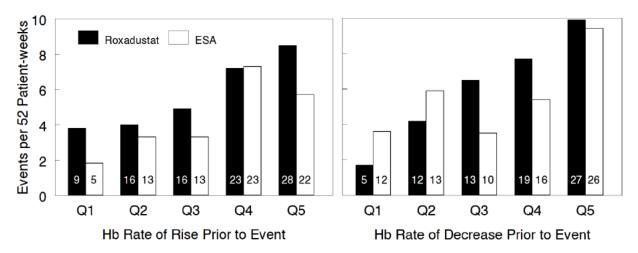
Figure 20: Thromboembolic Events vs. Hb Rate of Change Leading to Event—NDD Population



DD Patient Population

For the DD population, there were greater numbers of thromboembolic events for which a Hb slope could be calculated (Figure 21). There is a notable association between thromboembolic events and slope for both treatment groups, suggesting that measures to limit Hb rate of rise could decrease the frequency of thromboembolic events.

Figure 21: Thromboembolic Events vs. Hb Rate of Change Leading to Event—DD Population



Summary of Important Risks

Death

The results for all-cause mortality are difficult to interpret. In both the NDD and DD patient populations, the results of the meta-analyses are nearly neutral for the primary analyses, but nominally statistically significantly unfavorable for roxadustat in the sensitivity analyses. Specifically, for the NDD patient population, the estimated HR for the primary on-study analysis is 1.08, whereas there is a nominally statistically significant finding (not favoring roxadustat) for the OT+7 sensitivity analysis (HR = 1.40; 95% CI 1.08, 1.82). For the DD population, the estimated HR for the primary OT+7 analysis was 1.02, whereas the HR for the on-study sensitivity analysis was nominally statistically significant (HR 1.17, 95% CI 1.02,

1.35). Although Study 613 was not one of the studies in the meta-analysis, its mortality finding is a concern. In general, concordance between primary statistical analyses and sensitivity analyses provides confidence in the validity of the results. With the observed discordance here, the results are inconclusive.

Other important risks of MI, stroke, thrombosis, device/shunt thrombosis, systemic hypertension, seizure, and malignancy are summarized separately for the NDD and DD populations.

NDD Population

Table 30 summarizes the more important risks in the NDD patient population, as extracted from the principal data sources in the NDA. Note that the sample sizes and methods of expression differ among the sources. For studies 001, 060, and 068, the numbers in parentheses in the "Roxadustat" and "Comparator" columns represent rates per 100 P-Y. For study 610, the numbers in parentheses represent percent of subjects. Risk differences and relative risk are based on events per 100 P-Y for Studies 001, 060, 068, and percent of subjects for Study 610. For relative risk, the vertical dashed line is set to 1.0.

Table 30: Important Risks in the NDD Patient Population; Combined Data Sources

	Roxadustat	Comparator	Risk	Relative
			Difference	Risk
Myocardial Infarction			<u>-</u>	<u> </u>
Studies 001, 060, 068; MACE - On-study	86 (1.9)	52 (1.5)	0.4	1.3
Studies 001, 060, 068; MACE - OT+7	72 (1.9)	37 (1.6)	0.3	1.2
Studies 001, 060, 068; Serious AEs	54 (1.4)	31 (1.3)	0.1	1.1
Study 610	7 (2.2%)	8 (2.7%)	-0.5	0.8
Stroke			_	
Studies 001, 060, 068; MACE - On-study	56 (1.2)	36 (1.1)	0.1	1.3
Studies 001, 060, 068; MACE - OT+7	48 (1.2)	21 (0.9)	0.3	1.5
Studies 001, 060, 068; Serious AEs	53 (1.3)	26 (1.1)	0.3	1.2
Study 610	2 (0.6%)	5 (1.7%)	-1.1	0.4
Thrombosis			-	l į
Studies 001, 060, 068; Serious AEs	140 (3.6)	58 (2.5)	1.10	1.5
Studies 001, 060, 068; All AEs	195 (4.1)	76 (2.0)	2.10	2.0
Study 610; Serious AEs	20 (6.2%)	13 (4.4%)	1.80	1.4
Study 610; All AEs	25 (7.7%)	15 (5.1%)	2.60	1.5
Device/Shunt Thrombosis			•	
Studies 001, 060, 068; Serious AEs	36 (0.9)	8 (0.3)	0.60	2.7
Studies 001, 060, 068; All AEs	88 (1.8)	20 (0.5)	1.30	3.4
Systemic Hypertension			•	
Studies 001, 060, 068; Serious AEs	75 (1.9)	46 (2.0)	0.40	1.3
Studies 001, 060, 068; All AEs	411 (8.6)	224 (6.0)	2.60	1.4
Study 610; Serious AEs	9 (3%)	8 (3%)	0.00	1.0
Study 610; All AEs	87 (27%)	90 (31%)	-4.0	0.9
Seizures			•	l i
Studies 001, 060, 068; Serious AEs	9 (0.2)	1 (0)	0.20	5.4
Studies 001, 060, 068; All AEs	24 (0.5)	3 (0.1)	0.40	6.2
Study 610; Serious AEs	2 (0.6%)	0 (0%)	0.60	-
Malignancy			-	
Studies 001, 060, 068; Serious AEs	37 (1.0)	23 (1.0)	0.00	1.0
Studies 001, 060, 068; All AEs	43 (0.9)	34 (0.9)	0.00	1.0
Study 610; Serious AEs	9 (3%)	7 (2%)	0.40	1.2

Relative to placebo, there are signals for all of the thrombotic adverse events, particularly the thrombosis query (RR \cong 1.6) and device/shunt thrombosis (RR \cong 3). Seizures have a RR \cong 6. Malignancy is neutral. Myocardial infarction, stroke, and hypertension have RRs in the 1.2- to 1.3-range, which are difficult to interpret given the differential rates of dropout between subjects who received roxadustat and placebo.

Adverse Events by Subgroup

Table 31 shows adverse events in the OT+7 ascertainment window for four major risks by subgroup. The numbers in the table represent events per 100 P-Y. Relative risks (RR) are unitless. Continuous variables are shown in quartiles, e.g., age, body mass index (BMI), baseline Hb, and baseline GFR.

Table 31: Major Risks by Subgroup in the NDD Population (All Adverse Events; OT+7 Analysis)

Events per 100 P-Y	•			Thrombosis, all			Device/shunt thrombosis, occlusion, malfunction, stenosis			Sepsis			Seizure		
,	İ	Subjects	Rox	Pbo	RR	Rox	Pbo	RR	Rox	Pbo	RR	Rox	Pbo	RR	
All	All	100%	5.0	3.3	1.5	2.3	0.9	2.6	2.6	1.2	2.1	0.6	0.1	4.8	
Sex	Female	58%	4.8	2.7	1.8	2.5	8.0	3.2	2.4	8.0	3.0	0.7	0.1	4.7	
o ex	Male	42%	5.5	4.2	1.3	1.9	1.0	2.0	2.8	1.8	1.6	0.5	0.1	4.9	
	18-53	24%	3.7	1.8	2.1	3.4	1.4	2.4	2.0	8.0	2.5	1.0	0.4	2.4	
Baseline age	54-63	26%	5.9	4.3	1.4	2.4	0.9	2.9	2.4	1.2	2.0	0.6	0.0	-	
quartile	64-72	24%	5.3	3.5	1.5	2.0	0.5	3.9	3.5	1.0	3.5	0.5	0.0	-	
	73-100	25%	5.2	3.3	1.6	1.3	0.8	1.6	2.4	1.7	1.4	0.4	0.2	2.7	
Age ≥ 65	No	53% 47%	4.9 5.3	3.3	1.5	2.9	1.1 0.6	2.5 2.6	2.2 3.1	1.0	2.3	0.7 0.5	0.2	4.1	
	Yes			3.3	1.6	1.6				1.5	2.1		0.1	5.9	
Age≥75	No	79%	5.1	3.1	1.7	2.5	0.9	2.8	2.5	1.1	2.4	0.6	0.1	5.8	
	Yes	21%	4.7	3.9	1.2	1.4	0.7	1.9	2.7	1.7	1.6	0.5	0.2	2.8	
Dosalina DMI	15-22.78	25%	2.9	1.9	1.5	2.3	0.7	3.3	2.2	0.9	2.5	0.6	0.5	1.1	
Baseline BMI quartile	22.79-25.82 25.83-29.76	25%	5.2	4.4	1.2	2.0	0.8	2.4	3.2 2.8	1.0	3.1	0.4	0.0	-	
quartife	29.77-60.3	25% 25%	5.6 6.6	3.7 3.0	1.5 2.2	2.5 2.4	1.2 0.7	2.0 3.5	2.6	1.4 1.5	2.0 1.4	0.7 0.7	0.0 0.0	-	
	Asian	36%	3.5	2.6	1.3	1.7	0.4	4.7	3.0	1.6	1.9	0.6	0.1	4.9	
	Black	8%	4.9	4.3	1.1	1.2	1.4	0.9	1.8	0.9	1.9	1.2	0.0	-	
Race	Other	8%	5.2	1.5	3.4	1.0	0	-	2.6	0.5	5.2	0.7	0.0	_	
	White	47%	6.4	3.9	1.7	3.2	1.3	2.5	2.3	1.1	2.1	0.5	0.2	2.8	
	4.9-8.72	25%	5.8	4.3	1.3	3.0	0.9	3.5	4.0	1.9	2.1	0.8	0.2	3.7	
Baseline	8.73-9.23	25%	4.6	3.7	1.3	2.1	1.3	1.6	3.0	0.9	3.3	0.8	0.0	-	
hemoglobin	9.24-9.63	25%	5.2	2.7	1.9	2.1	0.3	6.6	2.3	1.3	1.8	0.3	0.3	1.0	
quartile	9.64-10.57	25%	4.7	2.8	1.7	2.0	1.0	2.0	1.2	0.9	1.3	0.6	0.0	-	
History of CV	No	68%	4.4	2.5	1.8	2.3	0.8	3.0	2.3	1.1	2.2	0.6	0.1	4.4	
disease	Yes	32%	6.4	4.9	1.3	2.3	1.1	2.2	3.1	1.5	2.2	0.8	0.1	5.8	
	1.6-11.07	25%	7.9	5.6	1.4	6.2	2.2	2.8	3.6	1.8	2.0	0.7	0.4	1.5	
Baseline eGFR	11.1-16.97	25%	6.5	3.5	1.9	2.5	1.1	2.3	2.6	1.1	2.4	0.5	0.0	-	
quartile	17.0-25.99	25%	3.0	3.3	0.9	0.5	0.7	8.0	1.6	1.0	1.6	0.7	0.2	4.3	
	26.0-75.2	25%	3.2	1.7	1.9	0.4	0	-	2.7	1.1	2.4	0.6	0.0	-	
History of	No	43%	4.9	3.1	1.6	3.2	1.5	2.1	1.8	1.0	1.8	0.6	0.3	1.9	
diabetes	Yes	57%	5.1	3.4	1.5	1.5	0.4	4.0	3.2	1.3	2.4	0.7	0.0	-	

Rox = roxadustat; Pbo = placebo; RR = relative risk; BMI = body mass index; eGFR = estimated glomerular filtration rate

For thrombosis (yellow column), the RRs are fairly consistent across subgroups; however, there are subgroups where risk trends higher. For example, a higher risk of thrombosis is evident in subjects with higher BMI, lower baseline Hb, and lower eGFR. The risk of sepsis (blue column) tends to be higher in

older subjects, as well as subjects with lower baseline Hb, lower baseline eGFR, and a history of CV disease or diabetes. Seizure risk (purple column) is higher in younger subjects. It is important to recognize that these are relatively small numbers of events; therefore, these estimates are subject to considerable uncertainty.

DD Population

Table 32 shows the important risks in the DD patient population. Note that the sample sizes and methods of expression differ among the sources. For studies 002, 063, and 064, the numbers in parentheses in the "Roxadustat" and "ESA" columns represent rates per 100 P-Y. For study 613, the numbers in parentheses represent percent of subjects. Risk differences and relative risk are based on events per 100 P-Y for Studies 002, 063, 064, and percent of subjects for Study 613. For relative risk, the vertical dashed line is set to 1.0. Note there are far more adverse events here than in the NDD subject population.

Table 32: Important Risks in the DD Patient Population

	Roxadustat	ESA	Risk Difference	Relative Risk
Myocardial Infarction			Difference	Nisk
Studies 002, 063, 064; MACE - OT+7	103 (3.1)	109 (3.0)	0.1	1.07
Studies 002, 063, 064; MACE - On-study	124 (3.2)	115 (2.8)	0.4	1.14
Studies 002, 063, 064; Serious AEs	88 (2.7)	85 (2.3)	0.4	1,2
Study 613	10 (2.4%)	17 (4.0%)	-1.6	0,6
Stroke				
Studies 002, 063, 064; MACE - OT+7	45 (1.4)	50 (1.3)	0.1	10
Studies 002, 063, 064; MACE - On-study	58 (1.5)	60 (1.4)	0.1	10
Studies 002, 063, 064; Serious AEs	51 (1.5)	49 (1.3)	0.2	1 2
Study 613	4 (1%)	8 (2%)	-0.9	0,5
Thrombosis			•	
Studies 002, 063, 064; Serious AEs	241 (7.3)	201 (5.4)	1.9	1,4
Studies 002, 063, 064; All AEs	392 (11.8)	344 (9.2)	2.6	13
Study 613; Serious AEs	52 (13%)	43 (10%)	2.4	1 2
Study 613; All AEs	77 (19%)	65 (16%)	3.1	1 2
Device/Shunt Thrombosis				į
Studies 002, 063, 064; Serious AEs	121 (3.7)	94 (2.5)	1.1	1,5
Study 613; Serious AEs	35 (9%)	22 (5%)	3.3	1,6
Systemic Hypertension				
Studies 002, 063, 064; Serious AEs	89 (2.7)	110 (2.9)	-0.30	0 ¦9
Studies 002, 063, 064; All AEs	365 (11.0)	367 (9.8)	1.20	1 1
Study 613; Serious AEs	13 (3%)	8 (2%)	1.20	1 2
Study 613; All AEs	79 (19%)	85 (20%)	-1.1	0 9
Seizures				į
Studies 002, 063, 064; Serious AEs	26 (0.8)	19 (0.51)	0.27	1,6
Studies 002, 063, 064; All AEs	45 (1.4)	33 (0.9)	0.50	15
Study 613; Serious AEs	2 (0.5%)	4 (1%)	-0.50	0 5
Malignancy			,	
Studies 002, 063, 064; Serious AEs	23 (0.7)	28 (0.8)	- 0. 1 0	0 ¦9
Studies 002, 063, 064; All AEs	42 (1.3)	48 (1.3)	0.00	10
Study 613; Serious AEs	15 (4%)	15 (4%)	0.00	10

Relative to epoetin alfa, there are signals for MI (RR \cong 1.1), thrombosis (RR \cong 1.3), device/shunt thrombosis (\cong 1.5), and seizures (RR \cong 1.5). Stroke, hypertension, and malignancy are neutral (again, however, relative to epoetin alfa, for which these are labeled adverse drug reactions).

Adverse Events by Subgroup

Table 33 shows adverse events in the OT+7 ascertainment window for four major risks by subgroup. The numbers in the table represent events per 100 P-Y. Relative risks (RR) are unitless. Continuous variables are shown in quartiles, e.g., age, body mass index (BMI), baseline Hb, and baseline GFR

Table 33: Major Risks by Subgroup in the DD Population (All Adverse Events; OT+7 Analysis)

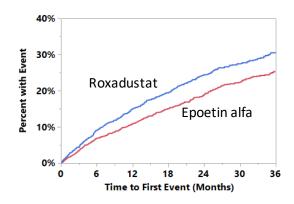
Events per Percent 100 P-Y of				Thrombosis, all		Device/shunt thrombosis, occlusion, malfunction, stenosis			Sepsis			Seizure		
	•	Subjects	Rox	EPO	RR	Rox	EPO	RR	Rox	EPO	RR	Rox	EPO	RR
All	All	100%	9.4	7.8	1.2	7.6	6.3	1.2	3.2	3.0	1.1	1.1	0.8	1.4
Sex	Female	58%	10.0	8.1	1.2	8.7	7.0	1.2	3.0	3.0	1.0	0.8	0.6	1.4
	Male	42%	8.9	7.7	1.2	6.9	5.8	1.2	3.3	3.0	1.1	1.2	0.9	1.5
Baseline age quartile	18-44 45-56 57-65 66-94	25% 26% 25% 24%	5.6 9.6 8.9 14.3	5.5 6.8 8.7 10 3	1.0 1.4 1.0 1.4	6.0 8.0 8.0 8.9	5.5 5.5 6.9 7.2	1.1 1.5 1.2 1.2	1.9 3.5 3.4 4.0	1.7 3.1 3.3 3.9	1.1 1.1 1.0 1.0	1.6 1.1 0.8 0.8	1.1 0.5 0.9 0.6	1.5 2.1 1.0 1.3
Age≥65	No	73%	7.8	7.0	1.1	7.2	5.9	1.2	2.9	2.7	1.1	1.2	0.8	1.4
	Yes	27%	14.2	10 3	1.4	9.0	7.4	1.2	4.0	3.9	1.0	0.8	0.5	1.5
Age≥75	No	91%	9.0	7.4	1.2	7.5	6.0	1.2	3.0	2.8	1.1	1.1	0.8	1.5
	Yes	9%	14.0	12 3	1.1	8.8	8.8	1.0	4.9	4.8	1.0	0.3	0.5	0.6
Baseline BMI quartile	14.6-22.83 22.83-26.37 26.37-30 9 31-64.9	25% 25% 25% 25%	8.2 8.5 8.5 12.1	5.2 7.7 7.8 10.4	1.6 1.1 1.1 1.2	6.2 7.4 6.8 9.8	4.5 5.7 7.0 7.7	1.4 1.3 1.0 1.3	2.6 2.8 2.8 4.5	2.2 2.5 3.1 4.1	1.2 1.1 0.9 1.1	1.2 1.1 1.2 0.8	0.6 0.9 0.7 0.8	2.0 1.2 1.8 1.0
Race	Asian	14%	7.5	5.1	1.5	5.0	4.3	1.2	3.4	4.3	0.8	1.7	0.8	2.2
	Black	18%	13.0	9.4	1.4	11.9	8.6	1.4	4.0	2.7	1.5	1.3	0.8	1.6
	Other	7%	6.1	5.6	1.1	5.6	4	-	4.3	3.2	1.3	2.2	1.9	1.2
	White	61%	9.0	8.1	1.1	7.0	6.1	1.2	2.8	2.9	1.0	0.8	0.7	1.2
Baseline hemoglobin quartile	4.3-8.8 8.8-9.8 9.8-10.66 10.67-12 2	25% 25% 25% 25%	8.2 10.0 10.5 8.8	7.0 8.2 9.6 6.5	1.2 1.2 1.1 1.3	7.3 8.9 7.3 7.2	5.7 6.5 7.8 5.1	1.3 1.4 0.9 1.4	2.3 3.1 3.5 3.5	1.7 2.5 4.7 2.9	1.4 1.2 0.7 1.2	1.6 1.0 1.0 0.8	0.5 0.8 1.0 0.7	3.2 1.3 1.0 1.1
History of CV	No	57%	7.4	5.5	1.3	6.5	4.7	1.4	2.2	2.3	0.9	1.1	0.7	1.6
disease	Yes	43%	12.2	11.0	1.1	9.2	8.4	1.1	4.6	4.0	1.1	1.0	0.8	1.2
Type of	HD	90%	9.9	8.2	1.2	8.3	6.7	1.2	3.3	3.0	1.1	1.0	0.7	1.5
Dialysis	PD	10%	4.4	4.2	1.1	1.6	2.1	0.7	1.6	3.1	0.5	1.6	1.3	1.2
History of diabetes	No	53%	7.0	6.4	1.1	6.5	5.5	1.2	1.9	2.0	0.9	1.0	0.5	1.8
	Yes	47%	12.4	9.6	1.3	9.1	7.2	1.3	4.7	4.2	1.1	1.2	1.0	1.2

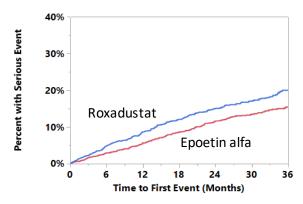
Rox = roxadustat; EPO = epoetin alfa; RR = relative risk; HD = hemodialysis; PD = peritoneal dialysis

For thrombosis (yellow column), the RRs are fairly consistent across subgroups; however, there are subgroups where risk trends higher. For example, a higher risk of thrombosis is evident in older subjects, subjects with higher BMI, subjects with a history of cardiovascular disease, subjects on hemodialysis, subjects with diabetes, and possibly females. The risk of device/shunt thrombosis (orange column) follows the same pattern. Note that for subjects on hemodialysis, the rates of device/shunt thrombosis, occlusion, malfunction, stenosis are 8.3 and 6.7 per 100 P-Y for roxadustat and epoetin alfa, respectively, for a risk difference of 1.6 events per 100 P-Y. The risk of sepsis (blue column) increases with age, BMI, a history of cardiovascular disease, diabetes, and hemodialysis (the latter for roxadustat only). Seizure risk (purple column) is higher in younger subjects and possibly subjects with low baseline Hb. It is important to recognize that these are relatively small numbers of events; therefore, these estimates are subject to considerable uncertainty.

Given the importance of thromboembolic events, we performed a Kaplan-Meier time-to-first thrombotic event analysis for the DD subject population (Figure 22) for all (left) and serious (right) events. The OT+7 ascertainment window was used for the analyses.

Figure 22: Time to First Thrombotic Event—All Events (Left); Serious Events (Right) for the DD Population (Studies 002, 063, and 064); OT+7 Ascertainment Window





Source: FDA analysis

The excess risk accrues continuously throughout the three studies.

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Appendix

Approved Epogen Label

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/103234s5369lbl.pdf (accessed 6/21/2021)

Adverse Event Preferred Terms Used in Key Queries

Table 34: Terms in Key Adverse Event Queries

Thursday	Device/shunt thrombosis/	Churcher
Thrombosis	occlusion/malfunction/stenosis	Stroke
Cerebral infarction	Thrombosis in device	Cerebral infarction
Embolic cerebral infarction	Arteriovenous fistula thrombosis	Embolic cerebral infarction
Ischaemic stroke	Arteriovenous graft thrombosis	Ischaemic stroke
Cerebellar infarction	Vascular access site thrombosis	Cerebellar infarction
Lacunar stroke	Vascular graft thrombosis	Lacunar stroke
Embolic stroke	Medical device site thrombosis	Embolic stroke
Brain stem stroke	Device occlusion	Brain stem stroke
Lacunar infarction	Arteriovenous fistula occlusion	Lacunar infarction
Thrombosis in device	Vascular access site occlusion	Cerebrovascular accident
Arteriovenous fistula thrombosis	Vascular access complication	Haemorrhagic stroke
Arteriovenous graft thrombosis	Vascular access malfunction	Brain stem haemorrhage
Vascular access site thrombosis	Arteriovenous graft site stenosis	
Vascular graft thrombosis	Shunt occlusion	Sepsis/septic shock
Graft thrombosis	Shunt malfunction	
Shunt thrombosis	Vascular graft stenosis	Device related sepsis
Acute myocardial infarction	Anastomotic stenosis	Enterococcal sepsis
Myocardial infarction	Vascular access site complication	Sepsis
Deep vein thrombosis	Vascular graft occlusion	Urosepsis
Thrombosis		Streptococcal sepsis
Atrial thrombosis	Device/shunt thrombosis	Pseudomonal sepsis
Peripheral artery thrombosis		Staphylococcal sepsis
Subclavian vein thrombosis	Thrombosis in device	Septic shock
Brachiocephalic vein thrombosis	Arteriovenous fistula thrombosis	Sepsis syndrome
Subclavian artery thrombosis	Arteriovenous graft thrombosis	Biliary sepsis
Vena cava thrombosis	Vascular access site thrombosis	Bacterial sepsis
Thrombophlebitis superficial	Vascular graft thrombosis	Fungal sepsis
Arterial thrombosis	Graft thrombosis	Citrobacter sepsis
Thrombophlebitis	Shunt thrombosis	Listeria sepsis
Jugular vein thrombosis	Medical device site thrombosis	Abdominal sepsis
Venous thrombosis	Device related thrombosis	Septic encephalopathy
Pelvic venous thrombosis	Injection site thrombosis	Escherichia sepsis
Venous thrombosis limb	-	•
Cardiac ventricular thrombosis	Seizure FDA	
Intracardiac thrombus		-
	Epilepsy	
	Epileptic encephalopathy	
	Seizure	
	Generalised tonic-clonic seizure	
	Idiopathic partial epilepsy	
	Partial seizures	
	Tonic convulsion	

EXHIBIT WW



FIBROGEN

ROXADUSTAT

[FG-4592]

HYPOXIA-INDUCIBLE FACTOR PROLYL HYDROXYLASE INHIBITOR FOR THE TREATMENT OF ANEMIA OF CHRONIC KIDNEY DISEASE

CARDIOVASCULAR AND RENAL DRUGS ADVISORY COMMITTEE

MEETING DATE: 15 JULY 2021

ADVISORY COMMITTEE BRIEFING MATERIALS: AVAILABLE FOR PUBLIC RELEASE

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ACM	All-cause mortality
AE	Adverse event
ANCOVA	Analysis of Covariance
AUC	Area under the curve
AVF	Arteriovenous fistula
AVG	Arteriovenous graft
BCRP	Breast cancer resistance protein
BMI	Body mass index
CI	Confidence interval
CKD	Chronic kidney disease
CLR	Renal clearance
C _{max}	Maximum plasma concentration
CV	Cardiovascular
CYP	Cytochrome P450
DD	Dialysis-dependent
DVT	Deep vein thrombosis
eGFR	Estimated glomerular filtration rate
EPO	Epoetin alfa
ESA	Erythropoiesis-stimulating agent
ESRD	End-stage renal disease
FAS	Full analysis set
FDA	Food and Drug Administration
Hb	Hemoglobin
HIF	Hypoxia-inducible factor
HIF-PH	Hypoxia-inducible factor prolyl hydroxylase
HR	Hazard ratio
HRQoL	Health-related quality of life
hsCRP	High-sensitivity C-reactive protein
ID (or ID-DD)	Incident dialysis
IERC	Independent Event Review Committee
ITT	Intent-to-treat
IV	Intravenous
KDIGO	Kidney Disease: Improving Global Outcomes
LDL	Low-density lipoprotein
LSMean	Least squares mean
MACE	Major adverse cardiovascular event (all-cause mortality, myocardial
	infarction, and stroke)
MACE+	MACE, plus hospitalization for unstable angina or congestive heart failure
MCID	Minimal clinically important difference
MI	Multiple imputation
NDA	New drug application
NDD	Non-dialysis-dependent
OAT	Organic anion transporter
OATP	Organic anion transporting polypeptide
OT+7	On-treatment plus 7 days
OT+28	On-treatment plus 28 days

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Abbreviation	Definition
PE	Pulmonary embolism
PEY	Patient exposure year
PK	pharmacokinetic
PRA	Panel reactive antibody
PY	Patient year
QoL	Quality of life
RBC	Red blood cell
SAE	Serious adverse event
SDD	Stable dialysis-dependent
SF-36	36-item short form questionnaire
TIW	3 times per week
TSAT	Transferrin saturation
UGT	uridine diphosphate-glucuronosyltransferase
ULN	Upper limit of normal
VAT	Vascular access thrombosis

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1. EXECUTIVE SUMMARY

1.1. Introduction

FibroGen, in global partnership with AstraZeneca and Astellas, is seeking approval of roxadustat (FG 4592) for the treatment of anemia in patients with chronic kidney disease (CKD) not on dialysis and on dialysis. Treatment with roxadustat is intended for the correction of anemia by increasing and maintaining hemoglobin (Hb) in patients with CKD. Roxadustat is a first-in-class, potent, orally active, and reversible inhibitor of hypoxia-inducible factor prolyl hydroxylase (HIF-PH) enzymes. By transiently inhibiting HIF-PH enzymes, roxadustat stimulates a coordinated erythropoiesis in a manner consistent with the natural physiologic response to hypoxia. Roxadustat presents a valuable option for the treatment of anemia to reduce the need for transfusion where the current standard of care leaves unmet needs.

The clinical development program for roxadustat in patients with CKD anemia included 9 Phase 2 studies, 8 United States (US) and Global Phase 3 studies, and 8 additional Phase 3 studies in Japan and China (Figure 1). In agreement with the Food and Drug Administration (FDA), safety data from the 3 pivotal placebo-controlled studies in non-dialysis-dependent (NDD) patients (Studies 001, 060, 608) were pooled and data from the 3 pivotal active-controlled studies in dialysis-dependent (DD) patients (Studies 002, 063, and 064) were pooled in their respective indications as they shared key study design elements and were global studies. Two additional global Phase 3 studies—Study 610 and Study 613 had different trial designs compared to the pivotal Phase 3 studies and were not included in the respective study pools; however, results from these studies are included in this document. Unlike the other NDD studies, Study 610 was open-label and used an active comparator (darbepoetin alfa) instead of placebo, and the study was ongoing at the time of the New Drug Application (NDA) submission. In contrast to the other DD studies which used epoetin alfa (EPO) as a comparator, Study 613 used both EPO and darbepoetin alfa as active comparators. The additional Phase 3 Studies 302, 307, 308, 310, 312, and 314 were conducted only in Japan and Studies 806 and 808 were conducted only in China and were not included in the respective study pools. These studies were of shorter duration, may not have had comparator arms, and did not have safety events adjudicated. A brief summary of the safety data generated from the studies conducted in China and Japan is provided in Section 9.

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Figure 1: Phase 2 and 3 Clinical Studies for the Development of Roxadustat for Patients with CKD Anemia



The data from more than 8,000 patients from the 6 pivotal studies demonstrated that roxadustat has a positive benefit-risk profile across the spectrum of CKD anemia in patients who are NDD and DD. The overall cardiovascular (CV) safety of roxadustat was shown to be comparable to placebo in patients with NDD CKD and to EPO in patients with DD CKD based on a comprehensive assessment of the roxadustat safety data via independent adjudication review. These findings support the use of roxadustat to safely increase Hb levels for patients with CKD anemia who need additional treatment options.

Roxadustat has been approved for DD and NDD CKD in China since 2018 and 2019, respectively, and in Japan since 2019 and 2020, respectively. Available post-marketing safety data have not shown any new unexpected risks.

1.2. Disease Background and Unmet Need

1.2.1. Overview of CKD Anemia

Anemia is common in patients with CKD – occurring in approximately 15% of patients with CKD in the US – and becomes increasingly severe as CKD progresses (Fishbane and Spinowitz 2018; Stauffer and Fan 2014). Anemia most commonly begins to develop when patients have between 20% and 50% of normal kidney function, and the majority of patients with a near total loss of kidney function, such as those with end-stage renal disease (ESRD), have anemia (Nakhoul and Simon 2016; St Peter et al 2018; USRDS 2020). Accordingly, approximately 50% of patients with Stage 4 to 5 CKD and more than 90% of patients with DD CKD are anemic (Nakhoul and Simon 2016).

Anemia is a condition marked by a deficiency in red blood cells (RBCs) (as measured by Hb levels) resulting in an inadequate oxygen-carrying capacity of blood to meet physiologic needs. The cause and extent of anemia may vary by age, sex, altitude, and smoking status (Stauffer and Fan 2014; WHO 2011). However, any disruption to erythropoiesis, such as that which occurs in CKD, has the potential to result in anemia.

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The Kidney Disease: Improving Global Outcomes (KDIGO) working group recommends that health care providers diagnose anemia in patients over 15 years old when Hb levels fall below 13 g/dL in males and 12 g/dL in females. Symptoms of anemia in patients with CKD often include low energy, fatigue, headache, impaired concentration, depression, impaired cognitive function, and overall reduced quality of life (QoL) (KDIGO Anemia Work Group 2012; Smith 2010). Additionally, anemia can reduce oxygen supply to the heart and cause increased heart rate and stroke volume, which may contribute to myocardial ischemia and lead to myocardial cell death. Anemia is associated with increased mortality and morbidity due to increased risk of CV hospitalization, all-cause- mortality (ACM), and progression of ESRD (Palaka et al 2020). Clinical changes due to acute anemia are generally reversible, but chronic anemia can lead to progressive and pathologic heart enlargement and left ventricular hypertrophy due to volume overload (Mozos 2015).

1.2.2. Pathophysiology of CKD Anemia

While anemia is defined by a decrease in Hb, its frequency and severity are complicated not only by the high degree of inflammation that patients with CKD experience but also by the effect of inflammation on currently available therapies. The etiology of anemia of CKD is complex and involves multiple pathological factors that impact erythropoiesis including: inflammation, which negatively affects multiple erythropoietic processes; elevated hepcidin, which restricts iron availability; and impaired oxygen sensing by the kidneys, which results in insufficient erythropoietin production by renal erythropoietin producing cells (specialized fibroblasts located between the renal tubules and capillaries in the cortex and outer medulla) (Shahbazi et al 2019). Inflammation contributes to the disrupted erythropoiesis that occurs in patients with CKD (Brugnara and Eckardt 2020; Icardi et al 2013; Nemeth and Ganz 2014; Shahbazi et al 2019). Increased inflammatory cytokines in CKD impairs production of erythropoietin and yields a reduced responsiveness or "hyporesponsiveness" to EPO-mediated differentiation and maturation of RBCs. As CKD progresses, erythropoietin production from REP cells is decreased to a level that is inadequate to maintain a normal rate of erythropoiesis (Fu et al 2016; Locatelli et al 2017; Souma et al 2016). As a result, Hb levels are reduced, causing anemia and systemic tissue hypoxia, and renal fibrosis may ensue (Shahbazi et al 2019). Additional factors that contribute to CKD anemia include chronic blood loss; iron, vitamin B12, or folic acid deficiency; and shortened RBC survival (from 120 days to 60–90 days) (Brugnara and Eckardt 2020).

1.2.2.1. Hepcidin and Iron Metabolism

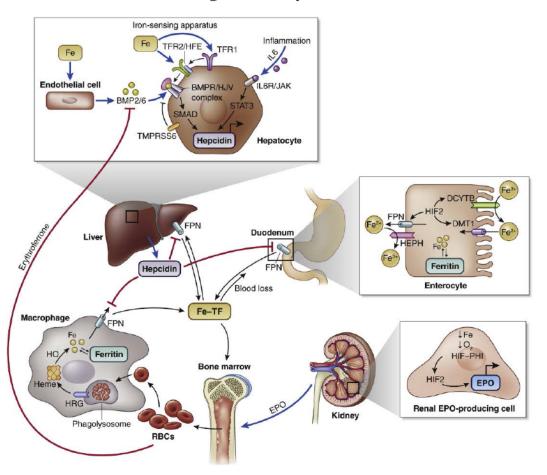
Several proteins, including ferritin and hepcidin, regulate iron levels in the body. Ferritin is an intracellular protein that stores iron and releases iron in a controlled fashion. Serum ferritin is elevated in patients with iron overload and decreased in patients with iron deficiency diseases (Jacobs et al 1972). Therefore, serum ferritin is used as an indirect marker of the total amount of iron stored in the body (Jacobs and Worwood 1975). However, factors such as inflammation, infection, and malignancy can elevate serum ferritin, which complicates the interpretation of serum ferritin levels (Wang et al 2010).

Hepcidin is a liver-derived key regulator of the entry of iron into the circulation (Ganz 2003). The role of hepcidin in regulation of systemic iron homeostasis is depicted in Figure 2. Hepcidin inhibits iron transport by binding to the iron export channel ferroportin, which is located on the surface of gut enterocytes, macrophages, and hepatocytes, leading to its internalization and degradation.

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When the hepcidin level is abnormally high (eg, because of inflammation), serum iron decreases because of iron trapping within macrophages and liver cells and decreased gut iron absorption. This decrease in serum iron can lead to anemia because there is an inadequate amount of serum iron available for developing RBCs. Increased hepcidin activity contributes to reduced iron availability seen in anemia of chronic inflammation, such as kidney failure (Ashby et al 2009). Hepcidin levels are controlled by multiple stimuli including iron stores (Mazur et al 2003), hypoxia (Shah and Xie 2014; Silvestri et al 2008), inflammation (Nemeth et al 2003), and erythropoiesis including erythropoiesis stimulated by erythropoietin therapy in renal disease (Ashby et al 2009; Nicolas et al 2002; Pak et al 2006).

Figure 2: Direct and Indirect Regulation of Systemic Iron Homeostasis



Abbreviations: DMT1=divalent metal transporter 1; EPO=erythropoietin; ERFE=erythroferrone; Fe=iron; FPN=ferroportin; HEPH=hephaestin; HFE=homeostatic iron regulator protein; HIF=hypoxia-inducible factors; HJV=hemojuvelin; HO=heme oxygenase; HRG=heme transporter HRG1; O2=oxygen; RBC=red blood cell transfusion; TF=transferrin; TFR1=transferrin receptor 1; TFR2=transferrin receptor 2; TMPRSS6=transmembrane serine protease 6. Source: Babitt et al 2021

High hepcidin levels result in iron sequestration in macrophages and hepatocytes (Zaritsky et al 2009) causing a clinical syndrome of functional iron deficiency. Clinically, this results in the need for high doses of IV iron to overcome the need for increasing doses of erythropoiesis-stimulating agents (ESAs) to achieve goal Hb levels (Goodnough et al 2010). The frequency by which patients receiving dialysis in the US experience this is represented by the fact that the mean ferritin levels (a marker of

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intracellular iron stores whose upper limit of normal [ULN] is frequently 300 mg/dL) is approximately 800 mg/dL according to the DOPPS Clinical Practice Monitor (Karaboyas et al 2020).

Some patients with CKD have an absolute iron deficiency, which is characterized by severely reduced or absent iron stores in the bone marrow, liver, and spleen. Absolute iron deficiency can arise from an increased rate of blood loss during dialysis, gastrointestinal bleeding from the combination of gastritis and platelet dysfunction (Liang et al 2014), or decreased gastrointestinal iron absorption and malnutrition.

1.2.3. Treatment of CKD Anemia

The objective of treatment for patients with NDD and DD CKD anemia includes increasing and maintaining Hb levels, reducing the risk of RBC transfusions, and enhancing QoL. Treatment of anemia in NDD and DD CKD is widely supported by worldwide guideline groups and regulatory approvals. Nephrologists typically diagnose anemia in patients with CKD, and the treatment has evolved significantly over the past 3 decades. In 1988, approximately 75% of dialysis patients in the US had a hematocrit of < 30%, indicative of severe anemia. During this time, patients undergoing dialysis routinely had Hb levels in the 5–6 g/dL range with marked symptomatology (Eschbach et al 1989; Eschbach et al 1987). The cumulative burden of associated symptoms led to the frequent administration of RBC transfusions. In 1989, this paradigm changed with the introduction of EPO, a first-in-class ESA that was approved via an orphan drug designation for the indication, "to elevate the red blood cell level [...] and to decrease the need for transfusions [...]" (Procrit Package Insert 2008). Subsequent uptake of ESAs was rapid and facilitated by a coverage determination from Medicare, and RBC transfusion became rescue therapy. ESA treatment that results in supraphysiologic erythropoietin levels and iron therapy remain the cornerstone of anemia treatment in patients with advanced CKD; nevertheless, rescue therapy with RBC transfusion is common.

The results of several large studies raised concerns about the use of ESAs to treat anemia in patients with CKD and about target Hb concentrations. These studies include:

- Normal Hematocrit Trial (1998)
- Correction of Hemoglobin and Outcomes in Renal Insufficiency (CHOIR) in 2006
- Trial to Reduce Cardiovascular Events with Aranesp Therapy (TREAT) in 2009

The results of these studies suggested that targeting higher Hb levels with higher doses of ESAs may contribute to CV adverse events (AEs). In 2011, the FDA published a safety announcement and implemented label changes for ESAs that included new warnings and called for more conservative ESA dosing in patients with CKD (FDA 2011). The new labels warned that, in controlled trials in CKD, patients experienced greater risks for death, serious CV AEs, and stroke when treated with ESAs to target a Hb level of > 11 g/dL. In addition, the labels warned that no trial had identified a Hb target level, ESA dose, or dosing strategy that did not increase these risks. Therefore, the recommendation was that healthcare providers should consider starting ESA treatment when Hb < 10 g/dL for patients with CKD. Dosing should be individualized, and the lowest dose of ESA sufficient to reduce the need for RBC transfusions should be used, after which dosing should be adjusted as appropriate. This recommendation did not define how far below 10 g/dL would be appropriate for an individual to initiate ESA treatment or the Hb level to target with treatment. Further, the recommendation was to reduce the dose or discontinue therapy when Hb rose above 10 g/dL in patients with NDD CKD.

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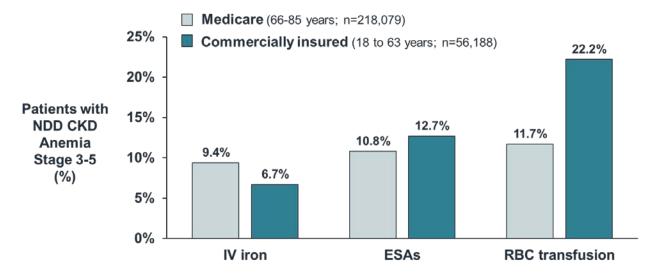
The KDIGO clinical practice guidelines for anemia in CKD were subsequently published in 2012, and these guidelines reflected the new FDA recommendations for ESAs. Each approved ESA product has a Boxed Warning for increased risk of death, myocardial infarction, stroke, venous thromboembolism, thrombosis of vascular access, and tumor progression or recurrence. Whereas these 2012 guidelines have attempted to mitigate the mortality and morbidity of anemia treatment in CKD, there has been limited subsequent innovation within the ESA category. New treatments have primarily been related to convenience through reducing the frequency of ESA injections, mainly in the NDD and home dialysis settings. There remains a significant unmet need for additional treatments for patients with CKD anemia, as reflected by a high rate of RBC transfusions in this patient population.

A further challenge in the treatment of CKD anemia is that many patients who are not on dialysis are not adequately treated for their anemia. Anemia treatment is initiated in a limited number of patients with NDD CKD, and treatment discontinuation is common in those who are treated due to the FDA labeled requirement to reduce or interrupt the ESA dose once a Hb level of 10 g/dL has been achieved (Davis et al 2020; St Peter et al 2018). In the US, fewer than 1 in 7 patients with NDD CKD were treated with an ESA in the 12 months prior to starting dialysis, and only 40% of patients with NDD CKD with Hb < 10 g/dL received any anemia medication within one year (St Peter et al 2018). Treatment with ESAs requires frequent clinic visits for many patients, from every week to monthly, depending on the prescribed ESA, as well as concurrent and not infrequent parenteral therapies. Particularly for patients who are not on dialysis, frequent travel to a healthcare facility is inconvenient or not even an option in underserved areas. A significant proportion of patients with NDD CKD are referred by their nephrologist to a hematologist due to the complexities and challenges of administering ESA and IV iron therapy, potentially impacting continuity of care. Accordingly, these patients are more likely than those without anemia to use healthcare resources, including hospitalizations and emergency department, hematologist, nephrologist, and outpatient (St Peter et al 2018).

The unmet need in patients with NDD CKD anemia is illustrated by the significant transfusion burden despite more than 30 years of ESA availability. Despite efforts including glycation and pegylation to increase ESA half-life and decrease dosing intensity, 40% of patients with NDD CKD require 1 or more RBC transfusions in the 2 years prior to the initiation of dialysis (Winkelmayer et al 2014). These findings support the concept that anemia is sub-optimally managed among patients with NDD CKD anemia in the real-world setting with a lack of sustained and efficacious treatment and a greater number of patients treated with RBC transfusions than ESAs on an annual basis in the US (St Peter et al 2018).

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Figure 3: Most Common Treatments Used in Patients with NDD CKD Anemia



Abbreviations: CKD=chronic kidney disease; ESA=erythropoiesis-stimulating agent; IV=intravenous; NDD=non-dialysis-dependent; RBC=red blood cell.

Source: St Peter et al 2018

Whereas RBC transfusions carry risks of volume overload, transfusion reactions, transmission of blood-borne infection, and iron overload, they only provide for a transient amelioration of anemia. Most importantly and of specific concern for patients with CKD, RBC transfusions are also associated with a decreased likelihood of receiving a kidney transplant, longer wait time prior to transplantation, and a higher risk of kidney rejection following transplantation due to allosensitization, the activation of the adaptive immune system to foreign antigens resulting in the generation of antibodies (Hickey et al 2016). This issue is critically important for patients with CKD, because kidney transplantation is associated with substantial improvements in survival and QoL (Gill et al 2005; Kostro et al 2016; Oniscu et al 2005; Wolfe et al 1999). The risk of allosensitization has been shown to increase with increasing number of transfusions, and allosensitization is associated with increased rejection and graft loss, as well as longer wait times to transplantation (Orandi et al 2016). In ESRD, panel reactive antibody (PRA) is commonly accepted as a routine practice in transplant centers and represents an estimate of alloimmunization. The incidence of rejection is significantly higher in patients with sensitization (ie, $PRA \ge 10\%$) than in patients without sensitization. Accordingly, the probability of receiving a kidney transplant is inversely related to the PRA percentage; for every percent increase in the PRA above 20%, the risk of not receiving a kidney transplant increased by 5% (Bostock et al 2013; Domingues et al 2010).

Therefore, a therapy that reduces the complexities of anemia treatment and decreases the incidence of RBC transfusions, including in patients with NDD CKD who are not currently treated for their anemia with ESA therapy, would be an important advance.

1.2.4. Unmet Need

Patients with CKD would benefit from an oral treatment for anemia that is safe, effective, and convenient and improves treatment across their entire clinical course. An ideal treatment would be efficacious across the spectrum of patients with NDD and DD CKD anemia including those with high levels of inflammation and inadequate clinical response to standard of care. The unmet need for

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additional treatments for CKD anemia is particularly apparent in patients who are incident to dialysis who are often hyporesponsive to ESA treatment due to inflammatory conditions, and patients undergoing home dialysis.

At the time of dialysis initiation in the US in 2018, patients had a mean Hb of 9.3 g/dL (USRDS 2018) due to limited use of ESAs, with less than 15% of patients treated for anemia of CKD contributing to the risk of transfusion that can affect their ultimate timing and success of transplantation. As would be expected in a population of patients who are generally untreated and who have low Hb at the time of dialysis initiation, rates of transfusion are highest in the 90 days following dialysis initiation, at nearly 150 transfusions/100 patient years (PY) (Wang et al 2016).

Inadequate response to ESAs is common and often due to inflammation and/or functional iron deficiency (Ganz 2003). Hyporesponsiveness is common in DD CKD, and patients who are hyporesponsive to ESAs require higher doses than non-hyporesponsive patients. Such high ESA doses have been associated with CV and thrombotic risk. ESA underperforms in those individuals with increased ferritin and hepcidin levels, indicative of clinical scenarios consistent with inflammation and functional iron insufficiency. These patients at present are devoid of clinical options beyond higher ESA doses, increased iron administration, or reliance on blood transfusion. Clinicians are regularly confronted with difficult treatment decisions in these patients who are inflamed or hyporesponsive, either opting for higher ESA doses with increased CV risk or lower ESA doses and increased requirement for RBC transfusion, which has its own risks and inconveniences. Relevantly, chronic ESA hyporesponders have approximately 7-fold higher monthly burden of RBC transfusion compared with patients who respond to ESA (Fishbane and Nissenson 2010; Kilpatrick et al 2008; Luo et al 2016; McCullough et al 2013).

The 2020 Advancing American Kidney Health Executive Order was a response to the challenges and barriers inherent in the care of individuals with CKD. The stated goal of this executive order is to "improve access to and quality of person-centered treatment options." Specifically, the executive order states, "We need to provide patients who have kidney failure with more options for treatment, from both today's technologies and future technologies such as artificial kidneys and make it easier for patients to receive care at home or in other flexible ways." The initiatives in this executive order include a number of measures meant to improve care and QoL for patients with CKD. Payment model adjustments were enacted to promote more widespread use of in-home dialysis, which is more convenient for patients than going into a dialysis center. More than 500,000 patients were on dialysis in 2016 and many of them spend 12 hours a week in dialysis centers (USRDS 2020).

In this context, the current standard of care with parenteral ESA therapy and regular administration of IV iron poses a burden for and a barrier to home hemodialysis and peritoneal dialysis. An oral therapy that can be self-administered in the home setting for hemodialysis and peritoneal dialysis patients will be a major advance in patient care, especially as more patients are treated in the home setting due to Centers for Medicare & Medicaid Services' objective to transition patients from in-center to home dialysis. Moreover, a therapy that reduces the requirement for IV iron in these home-treated patients will be an important clinical advance.

In summary, an ideal treatment for CKD anemia will be efficacious and IV iron mitigating or sparing and safe across the spectrum of NDD and DD CKD, including in patients with high levels of inflammation, inadequate iron mobilization, and inadequate clinical response to the current standard of care. An effective and convenient oral treatment can address the logistical challenges that many patients experience including IV access placement, need to travel to an infusion center, and increased

frequency of medical encounters; mitigate IV iron requirements and transfusion burden; and offer a more equitable access to therapy providing many patients on home dialysis and patients not on dialysis the opportunity to have appropriately managed anemia of CKD. Furthermore, a treatment with a novel mechanism of action that provides a "coordinated erythropoiesis," better reduces hepcidin, and improves iron bioavailability would empower personalized care aligned with patients' and healthcare providers' goals and more effectively treat CKD anemia.

1.3. Efficacy of Roxadustat in Patients with NDD CKD Anemia

1.3.1. Study Design

All 3 NDD studies (060, 608, and 001) were similarly designed, multicenter, randomized, double-blind, placebo-controlled trials (Table 1). Adult male and female patients with CKD Stage 3–5, estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m², and Hb \leq 10.0 g/dL at baseline were enrolled globally. Patients were randomized 2:1 to roxadustat and placebo in Studies 608 and 060 and 1:1 in Study 001. Target Hb with roxadustat treatment was 10–12 g/dL, and treatment duration was up to 4 years. The primary efficacy endpoint for all 3 studies was the mean change in Hb from baseline to mean over Weeks

28 to 52 regardless of rescue therapy (ie, RBC transfusion, ESA use, and intravenous [IV] iron supplementation). Secondary efficacy endpoints included the proportion of Hb responders (ie, Hb level of ≥ 11 g/dL with an increase of 1 g/dL for patients with baseline Hb > 8 g/dL and an increase of 2 g/dL for patients with baseline Hb ≤ 8 g/dL) without rescue, use of rescue therapy (ie, RBC transfusion, ESA use, and IV iron supplementation), RBC transfusion, change in hepcidin and iron parameters, and health-related quality of life (HRQoL). Given the similar study designs, the efficacy results for these studies were pooled for the NDA and are presented as such in this briefing document.

Table 1: Overview of NDD Study Designs

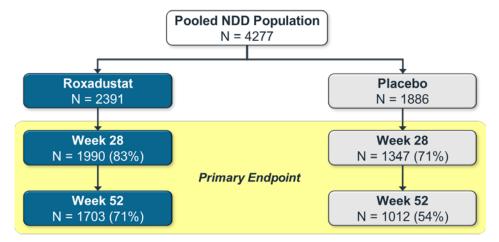
	Pivotal Phase 3 NDD Studies				
	Study 001	Study 060	Study 608		
Region	Global	Global	Global		
Randomized, double-blind	Yes	Yes	Yes		
Control	Placebo	Placebo	Placebo		
Baseline Hb	< 10.0 g/dL	≤ 10.0 g/dL	≤ 10.0 g/dL		
Randomization scheme	1:1	2:1	2:1		
Duration (years)	1 – 4	1 – 4	1 – 2		

Abbreviations: Hb=hemoglobin; NDD=non-dialysis-dependent.

1.3.2. Patient Disposition and Demographics

A total of 4,270 eligible patients from the 3 pivotal Phase 3 studies were randomized to roxadustat (N=2,386) or placebo (N=1,884) and received at least 1 dose of study treatment. Overall, 82% of patients in the roxadustat group and 71% of patients in the placebo group completed study treatment to the period during which the primary efficacy endpoint could be assessed (Figure 4). Because the primary efficacy endpoint is change from baseline to Week 28–52, it is relevant to present information as to how many patients continued treatment to these timepoints.

Figure 4: Pooled NDD Studies: Patient Disposition



Abbreviation: NDD=non-dialysis-dependent.

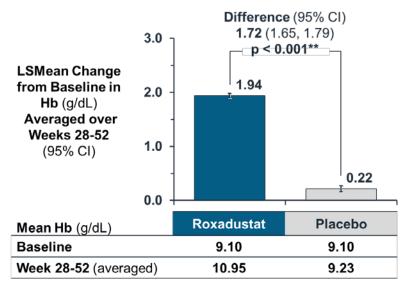
Baseline demographics and disease characteristics were similar between groups and were reflective of patients with NDD CKD globally. The mean age was approximately 62 years old, and baseline disease characteristics were similar between treatment groups. Baseline Hb was 9.10 g/dL, and a similar proportion of patients had Hb levels < 8.0 at baseline. Baseline eGFR was < 15 mL/min/1.73 m² in 42.5% of patients, and < 10 mL/min/1.73 m² in 19.6% of patients. Additional details are provided in Section 5.1.2.

1.3.3. Efficacy Results

The pre-specified primary efficacy endpoints were met in each individual study. Approval for efficacy is based on individual studies. To facilitate the presentation of efficacy, pooled results are presented rather than each of the individual studies where the results of individual studies were similar in terms of direction and magnitude. The reader should be reminded that while individual studies were controlled for multiplicity, this was not employed in the pooled analyses.

In the pooled analysis, the roxadustat group showed an improvement in mean Hb levels regardless of rescue therapy (ie, RBC transfusion, ESA use, and IV iron supplementation) compared to placebo (Figure 5).

Figure 5: Pooled NDD Studies: Mean Change in Hb from Baseline to Mean Over Weeks 28 to 52 Regardless of Rescue Therapy*



Abbreviations: CI=confidence interval; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; IV=intravenous(ly); LS=least square: NDD=non-dialysis-dependent; RBC=red blood cell.

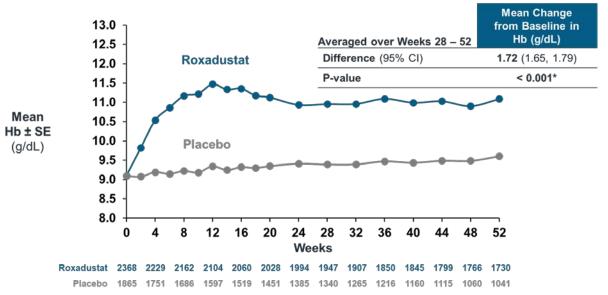
Note: Intent-to-treat analysis set.

Figure 6 compares the mean Hb over time, up to Week 52, between the pooled roxadustat and placebo groups in patients with NDD CKD. In the pooled roxadustat group, Hb increased starting from Week 2 through Week 12, following which the mean Hb level stabilized and was maintained close to 11.0 g/dL through the rest of the study period. By contrast, in the pooled placebo group, Hb levels remained relatively flat and close to baseline (approximately 9.0 g/dL) up to Week 52.

^{*}Rescue therapy included RBC transfusion, ESA use, and IV iron supplementation.

^{**}P-value not controlled for multiplicity.

Figure 6: Pooled NDD Studies: Mean (±SE) Hb (g/dL) over Time up to Week 52



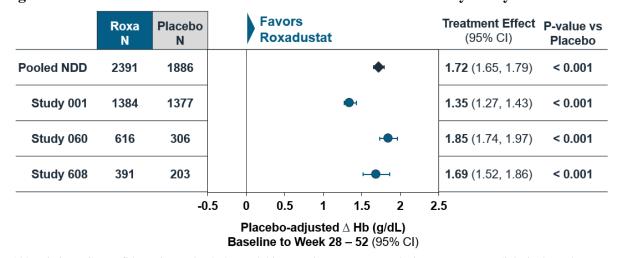
Abbreviations: CI=confidence interval; Hb=hemoglobin; NDD=non-dialysis-dependent; SE=standard error.

Note: Full analysis set.

*p-value not controlled for multiplicity.

Importantly, statistically and clinically significant improvements from baseline in mean Hb levels were seen across the 3 individual NDD studies. As shown by the placebo-adjusted treatment effect for roxadustat in Figure 7, the treatment effect for each of the pivotal studies in patients with NDD CKD was statistically significant compared to placebo.

Figure 7: Pooled NDD Studies: Roxadustat Treatment Effect by Study



Abbreviations: CI=confidence interval; Hb=hemoglobin; ITT=intent-to-treat analysis set; NDD=non-dialysis-dependent; OT+7=on-treatment plus 7 days; Roxa=roxadustat.

Note: Study 001 was analyzed using the ITT observational period; Studies 060 and 608 were analyzed using OT+7.

Additionally, the treatment effect consistently favored roxadustat across a wide range of pre-specified subgroups including region, sex, baseline high-sensitivity C-reactive protein (hsCRP), and eGFR range (Figure 8). Patients with the lowest eGFR at baseline had the lowest Hb levels at baseline, and therefore had a greater change from baseline than patients with higher eGFR at baseline.

Figure 8: Pooled NDD Studies: Roxadustat Treatment Effect by Subgroup

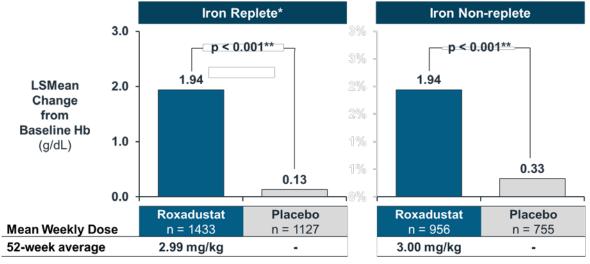
	Roxa N	Placebo N		Favors Roxadustat	Treatment Effect (95% CI)	P-value vs Placebo
Pooled NDD	2391	1886		•	1.72 (1.65, 1.79)	< 0.001
US	552	441		⊢● -1	1.61 (1.48, 1.74)	< 0.001
Europe	597	447		⊢ ⊕ ⊣	1.65 (1.53, 1.77)	< 0.001
Other	1242	998		⊢	1.62 (1.48, 1.77)	< 0.001
Male	974	832		₩-	1.72 (1.61, 1.84)	< 0.001
Female	1417	1054		l ⊕ l	1.73 (1.64, 1.82)	< 0.001
CRP ≤ ULN	1222	855		₽ <mark>⊕</mark> ₽	1.74 (1.65, 1.82)	< 0.001
CRP > ULN	526	357		⊢	1.67 (1.53, 1.82)	< 0.001
eGFR < 10*	481	359		⊢	1.99 (1.79, 2.19)	< 0.001
eGFR 10 - < 15*	526	452		⊢	1.85 (1.71, 1.98)	< 0.001
eGFR 15 - < 30*	954	724		⊢⊕⊣	1.65 (1.54, 1.76)	< 0.001
eGFR ≥ 30*	430	351		⊢●	1.46 (1.28, 1.64)	< 0.001
-0.5 0 0.5 1 1.5 2 2.5 Placebo-adjusted △ Hb (g/dL) Baseline to Week 28 – 52 (95% CI)						

Abbreviations: CI=confidence interval; CRP=C-reactive protein; eGFR=estimated glomerular filtration rate; Hb=hemoglobin; NDD=non-dialysis-dependent; Roxa=roxadustat; ULN=upper limit of normal; US=United States.

Note: Intent-to-treat analysis set.

Patients treated with roxadustat demonstrated a consistent Hb response irrespective of iron repletion status at baseline (Figure 9). Patients who were not iron replete (ie, ferritin < 100 ng/mL or TSAT < 20%) at baseline had similar change from baseline in Hb levels as those who were iron replete while utilizing similar doses of roxadustat and without requiring more transfusions or IV iron.

Figure 9: Pooled NDD Studies: LSMean Change from Baseline in Hb Levels in Patients Who Were Iron Replete* vs Iron Non-replete at Baseline



Abbreviations: Hb=hemoglobin; LS=least square; NDD=non-dialysis-dependent; TSAT=transferrin saturation.

^{*}mL/min/1.73 m²

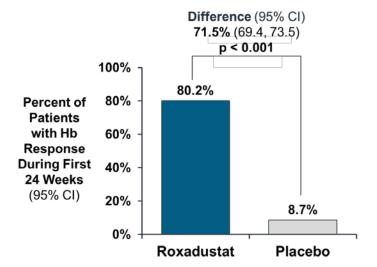
^{**}p-value not controlled for multiplicity.

^{*}Iron replete was defined as TSAT \geq 20% and ferritin \geq 100 ng/mL; mean change from baseline to mean of Weeks 28 to 52.

^{**}P-value not controlled for multiplicity.

As shown in Figure 10, a higher percentage of roxadustat-treated patients achieved Hb response (defined as Hb \geq 11.0 g/dL and increase by \geq 1.0 g/dL in patients with baseline Hb > 8.0 g/dL, or Hb increase by \geq 2.0 g/dL in patients with baseline Hb \leq 8.0 g/dL) during the first 24 weeks compared to placebo, with a treatment difference of 71.5% without rescue.

Figure 10: Pooled NDD Studies: Proportion of Patients with Hb Response



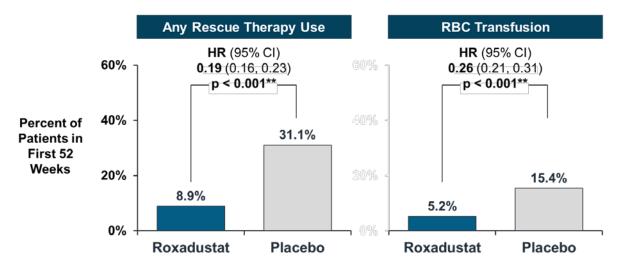
Baseline	Response Criteria
Hb > 8.0 g/dL	Hb ≥ 11.0 and Increase by ≥ 1.0
Hb ≤ 8.0 g/dL	Increase by ≥ 2.0

Abbreviations: CI=confidence interval; Hb=hemoglobin; NDD=non-dialysis-dependent. Note: Censored for rescue therapy.

Fewer patients from the roxadustat treatment group required any rescue therapy (ie, RBC transfusion, ESA use, or IV iron) or RBC transfusion compared to the placebo group during the first 52 weeks of treatment (Figure 11). A total of 124 patients (5.2%) in the roxadustat group required RBC transfusion compared to 288 (15.4%) in the placebo group, corresponding to an incidence rate of 6.1 patients with transfusion per 100 PY for roxadustat, and 20.4 per 100 PY for placebo.

^{*} P-value not controlled for multiplicity.

Figure 11: Pooled NDD Studies: Patients Receiving Any Rescue Therapy* or RBC Transfusion During the First 52 Weeks

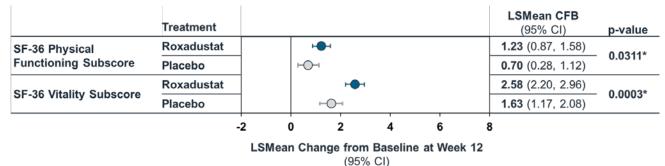


Abbreviations: CI=confidence interval; ESA=erythropoiesis-stimulating agent; HR=hazard ratio; IV=intravenous(ly); NDD=non-dialysis-dependent; RBC=red blood cell.

Note: Full analysis set.

HRQoL was assessed using patient-reported outcome measures. The physical functioning and vitality domains of the SF-36 v2 were included as secondary endpoints in the pooled analysis (Figure 12). Both roxadustat and placebo-treated patients reported least squares mean (LSMean) increases from baseline to Week 12 across all HRQoL endpoints. The difference between roxadustat and placebo-treated patients did not meet minimal clinically important difference (MCID) thresholds in any of the studies.

Figure 12: Pooled NDD Studies: LSMean Change from Baseline in Health-Related Quality of Life Scores at Week 12



Abbreviations: CI=confidence interval; CFB=change from baseline; LS=least square; NDD=non-dialysis-dependent; SF-36=36-item short form survey.

Note: Full analysis set.

1.3.4. Supportive Phase 3 NDD Study 610

In addition to the 3 pivotal NDD CKD placebo-controlled studies, Study 610 was a Phase 3 study to evaluate the roxadustat efficacy and safety in patients with NDD CKD with an active control,

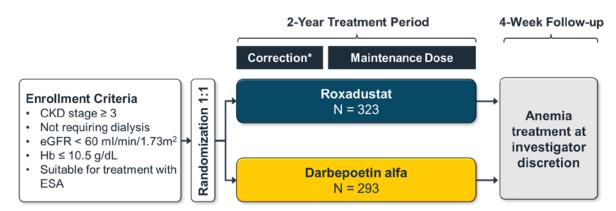
^{*}Rescue therapy included RBC transfusion, ESA use, and IV iron supplementation.

^{**}P-value not controlled for multiplicity.

^{*}p-value not controlled for multiplicity.

darbepoetin alfa (Figure 13). Study 610 was not pooled for analysis with the other NDD CKD studies because it used an active control and remains as a stand-alone study.

Figure 13: Study 610 Design



Abbreviations: CKD=chronic kidney disease; eGFR=estimated glomerular filtration rate; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin.

A total of 930 patients were screened and 616 were randomized to receive treatment, 323 to the roxadustat treatment group and 293 to the darbepoetin treatment group. Those patients are included in the Intent-To-Treat (ITT) and Safety Populations for statistical analysis.

Baseline demographics were comparable between the roxadustat and darbepoetin treatment groups, with mean age (66.8 in roxadustat vs 65.7 in placebo), and mean body mass index (BMI) (27.95 vs 28.74). The majority of patients were White (95.3% overall) and were randomized in Central and Eastern Europe (70.1%). Median baseline Hb was 9.68 g/dL for the roxadustat treatment group and 9.70 g/dL in the darbepoetin treatment group. Median baseline eGFR (17.5 mL/min/1.73 m² vs 18.5 mL/min/1.73 m²) was comparable between groups and was < 30 mL/min/1.73 m² for 82.5% patients overall (81.7% roxadustat vs 83.3% darbepoetin).

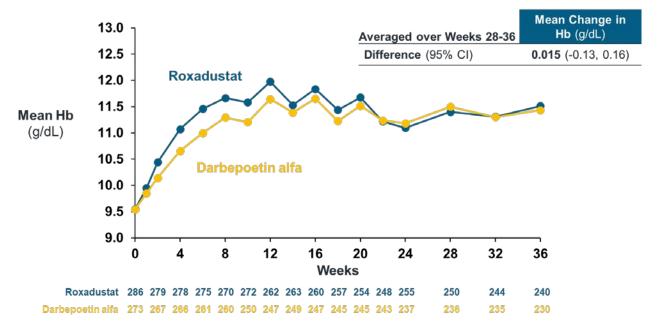
Treatment duration was considered comparable between treatment groups (median 103.71 weeks in the roxadustat treatment group vs 100.14 weeks in the darbepoetin treatment group). Total patient exposure years (PEY) on treatment was greater in the roxadustat treatment group (519.3 years) than the darbepoetin treatment group (472.5 years), because of the greater number of patients in the roxadustat treatment group.

<u>Primary Endpoint: Percentage of Hb Responders during the First 24 Weeks of Treatment Without Rescue Therapy</u>

In general, the efficacy data from Study 610 was consistent with other pooled pivotal studies. After 12 weeks, mean Hb levels stabilized and were comparable between treatment groups. In addition, mean Hb levels averaged over Weeks 28 to 36 demonstrated noninferiority of roxadustat to darbepoetin alfa (Figure 14).

^{*}Duration of correction phase is variable in length for each patient depending on when they reach $Hb \ge 11.0 \text{ g/dL}$ and an Hb increase from baseline $Hb \ge 1.0 \text{ g/dL}$

Figure 14: Study 610: Mean Change in Hb Levels Over Time



Abbreviations: CI=confidence interval; Hb=hemoglobin.

Note: Per protocol analysis set.

Hb Change from Baseline to Average Hb in Weeks 28 to 36 Without Rescue Therapy

The LSMean change was 1.85 (95% confidence interval [CI]: 1.75, 1.96) g/dL for patients in the roxadustat group and 1.84 g/dL (95% CI: 1.73, 1.94) for patients in the darbepoetin alfa group. The LSMean difference for roxadustat vs darbepoetin alfa was 0.015 g/dL (95% CI: -0.13, 0.16), signifying noninferiority of roxadustat to darbepoetin alfa based on a margin for noninferiority of > -0.75 g/dL.

Time to First IV Iron Use During First 36 Weeks

Significantly fewer patients in the roxadustat treatment group required IV iron use during the first 36 weeks. The incidence rate per 100 PY at risk was lower in the roxadustat group (9.9) compared with the darbepoetin alfa group (21.2), and the hazard ratio (HR) was 0.45 (95% CI: 0.26, 0.78; p=0.004).

Table 2: Study 610: IV Iron Use During the First 36 Weeks

	Roxadustat	Darbepoetin Alfa		
	N=322	N=292		
Patients with IV Iron	20 (6.2%)	37 (12.7%)		
Cumulative Time at Risk (PY)	201.8	174.5		
Incidence Rate (Per 100 PY)	9.9	21.2		
Hazard Ratio (95% CI), p-value	0.45 (0.26, 0.78), P=0.004			

Abbreviations: HR=hazard ratio; IV=intravenous(ly); PY=patient years.

1.4. Efficacy of Roxadustat in Patients with DD CKD Anemia

1.4.1. Study Design

The 3 pivotal DD studies (063, 064, and 002) were similarly designed, multicenter, randomized, open-label, clinical trials assessing the efficacy and safety of roxadustat compared with EPO (Table 3). Adult male and female patients with CKD on dialysis with threshold Hb < 10.0 g/dL at baseline (if not on ESA), and < 12.0 g/dL (if on ESA) were enrolled globally. Patients in these studies were randomized 1:1 to roxadustat and EPO. Target Hb was 10–12 g/dL with roxadustat treatment and as labeled for EPO, and the study durations were up to 4 years.

These studies included a pre-specified subpopulation of incident dialysis (ID) patients (ie, patients who started dialysis within \leq 4 months of study participation). The subpopulation of patients with ID-DD CKD consisted of all patients from Study 063 and a subset of eligible patients from Study 002 and Study 064 (14.1% and 9.6%, respectively).

The primary endpoint in all 3 studies was the same as that in the NDD studies: mean change from baseline in Hb to mean over Weeks 28 to 52, regardless of rescue therapy (ie, RBC transfusion and ESA). Secondary endpoints included Hb change by baseline inflammatory status (hsCRP > ULN) – because of the known underperformance of EPO in patients who are inflamed – as well as RBC transfusion, and IV iron use. Hepcidin and serum iron storage parameters were investigated as exploratory endpoints.

Table 3: Overview of DD Study Designs

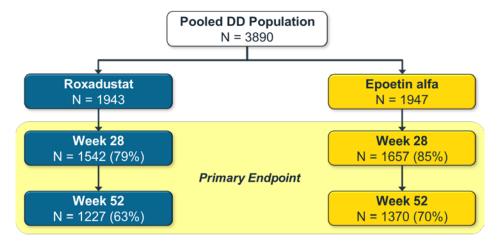
]	Pivotal Phase 3 DD Studies				
	Study 002	Study 063	Study 064			
Region	Global	Global	United States			
Design	Open-label	Open-label	Open-label			
Control	Epoetin alfa	Epoetin alfa	Epoetin alfa			
Randomization scheme	1:1	1:1	1:1			
Duration (years)	≤4 years	≤4 years	≤4 years			
Baseline Hb (g/dL)	< 12 if on ESA	< 10	9.0 – 12 (DD)			
	or < 10	≤ 10	8.5 – 12 (ID-DD)			

Abbreviations: DD=dialysis-dependent; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; ID-DD=incident dialysis-dependent.

1.4.2. Patient Disposition and Demographics

A total of 1943 patients were randomized in the roxadustat group and 1947 in the EPO group for a total of 3,890 patients who were included in the ITT set (Figure 15). A total of 1940 patients in each group received at least 1 dose of study drug and were included in the Safety Analysis Set. The ID-DD subpopulation consisted of 1,530 patients, and the stable dialysis-dependent (SDD) subpopulation consisted of 2,360 patients. Overall, 79.4% of patients in the roxadustat group and 85.1% of patients in the EPO group completed treatment to the period during which the primary endpoint was assessed.

Figure 15: Pooled DD Studies: Patient Disposition



Abbreviations: DD=dialysis-dependent.

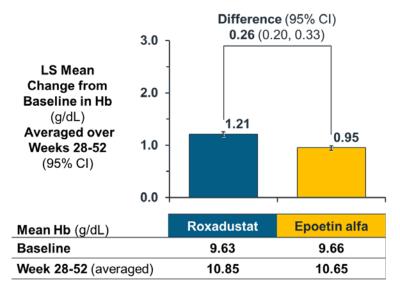
Baseline demographics were similar between the groups and are reflective of the underlying population of patients with DD CKD globally. The mean age of patients was approximately 55 years and ranged from 18 to 94 years. While globally, 61% of patients were White, approximately 18% were Black, and 14% were Asian, and among patients enrolled in the US, 40% were African American.

Approximately half of patients had diabetes. More than 90% utilized hemodialysis as their modality and 10% utilized peritoneal dialysis. Mean baseline Hb was approximately 9.6 g/dL, and a similar proportion of patients had Hb levels of < 10 at baseline in each group. Among patients with baseline hsCRP (n=3,246), the mean hsCRP at baseline was also similar between the groups, with a similar proportion of patients with hsCRP above ULN. Mean baseline iron parameters including hepcidin, transferrin saturation (TSAT) and ferritin were also comparable between groups. Additional details on baseline demographics are provided in Section 5.2.2.

1.4.3. Efficacy Results

The pre-specified primary efficacy endpoints were met in each individual study (Figure 17). To summarize these studies, pooled results are presented below. In the pooled analysis, the effect including the 95% CI of roxadustat was within the pre-specified non-inferiority margin (-0.75 g/dL), thereby demonstrating noninferiority compared to EPO on mean change from baseline in Hb over Weeks 28 to 52 regardless of rescue therapy (ie, RBC transfusion and ESA) (Figure 16).

Figure 16: Pooled DD Studies: Mean Change in Hb from Baseline to Mean Over Weeks 28 to 52 Regardless of Any Rescue Therapy*

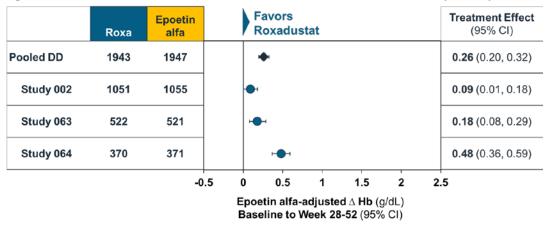


Abbreviations: CI=confidence interval; DD=dialysis-dependent; Hb=hemoglobin; LS=least square.

Note: Intent-to treat analysis set.

Importantly, the Hb response with roxadustat was consistent across the DD studies, with a non-inferior treatment effect of roxadustat compared to EPO in each individual study (Figure 17).

Figure 17: Pooled DD Studies: Roxadustat Treatment Effect by Study

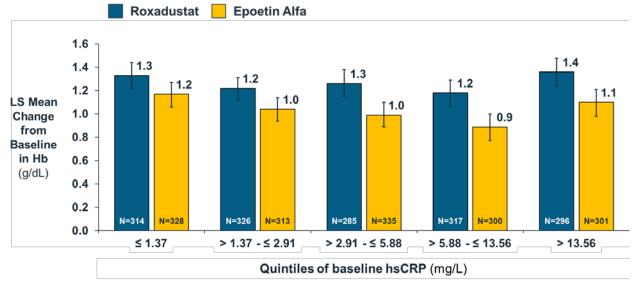


Abbreviations: CI=confidence interval; DD=dialysis-dependent; Hb=hemoglobin; Roxa=roxadustat. Note: Intent-to treat analysis set; non-inferiority margin=-0.75.

The ability of roxadustat to maintain Hb in the presence of inflammation likely related to its mechanism of action is an important clinical differentiator from ESA. While the treatment difference is clinically similar between roxadustat and EPO as quintiles of patients based on CRP are examined (Figure 18), roxadustat doses did not increase with increasing baseline hsCRP levels (Figure 19). In contrast, EPO dose requirements increased with increasing baseline hsCRP levels, reflecting the likely effect of inflammation on EPO dosing that is not affected in roxadustat dosing.

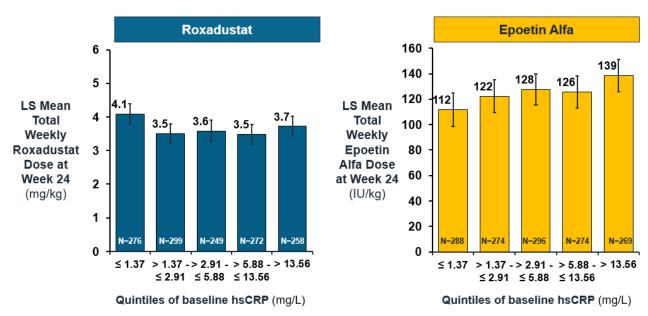
^{*}Rescue therapy consisted of red blood cell transfusion and erythropoiesis-stimulating agent.

Figure 18: Pooled DD Studies: Mean Hb Change from Baseline by hsCRP Quintiles at Baseline



Abbreviations: DD=dialysis-dependent; Hb=hemoglobin; hsCRP=high-sensitivity C-reactive protein; LS=least square. Note: Intent-to-treat analysis set.

Figure 19: Pooled DD Studies: Mean Weekly Study Drug Doses by Baseline hsCRP Quintiles

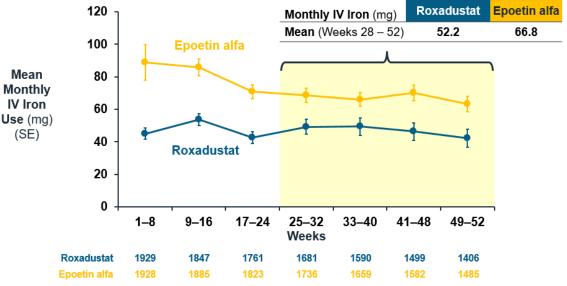


Abbreviations: DD=dialysis-dependent; hsCRP=high-sensitivity C-reactive protein; LS=least square. Note: Intent-to-treat analysis set

As shown in Figure 20, roxadustat-treated patients received less monthly IV iron than patients treated with EPO (p < 0.0001). In the Phase 3 studies, IV iron supplementation was permitted if the investigator thought that the patient had not responded adequately while taking oral iron or could not tolerate oral iron and was considered iron deficient as determined by either ferritin < 100 ng/ml or TSAT < 20%. On average, roxadustat-treated patients required 52 mg of IV iron over Weeks 28 to 52 compared to 67 mg iron required by EPO-treated patients. The difference in IV iron needs to be

interpreted in the context of patients in the roxadustat arm achieving numerically higher Hb levels with fewer transfusions. This is supportive of the Phase 2 Study 053 in which patients receiving roxadustat treated with oral iron were able to achieve and maintain similar Hb levels and similar iron stores as compared to those treated with IV iron (Besarab and Szczech 2014).

Figure 20: Pooled DD Studies: Average Monthly IV Iron Use Per Patient Exposure Month Over Weeks 28 to 52 (Full Analysis Set)

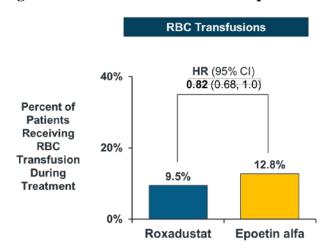


 $Abbreviations: DD = dialysis - dependent; \ IV = intravenous(ly); \ SE = standard \ error.$

Note: Full analysis set.

Numerically fewer patients treated with roxadustat required RBC transfusions compared with EPO, demonstrating non-inferiority between roxadustat and EPO (Figure 21).

Figure 21: Pooled DD Studies: Requirement for RBC Transfusion During Treatment

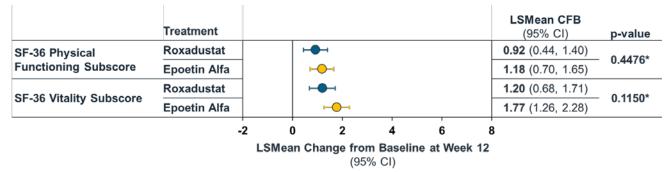


Abbreviations: CI=confidence interval; DD=dialysis-dependent; HR=hazard ratio; RBC=red blood cell. Note: Full analysis set.

The physical functioning and vitality domains of the 36-item short form questionnaire (SF-36) v2 were included as secondary endpoints in one of the studies and were exploratory endpoints in the other

study (Figure 22). Both roxadustat and EPO-treated patients reported LSMean increases from baseline to Week 12 across all HRQoL endpoints in the pooled analysis. There was no clinically meaningful difference between patients on roxadustat compared to EPO in the pooled analysis. This finding is expected as patients in both treatment arms experienced corrected Hb levels, leading to improved HRQoL compared with baseline. LSMean treatment differences between roxadustat and EPO-treated patients did not meet MCID thresholds.

Figure 22: Pooled DD Studies: LSMean Change from Baseline in Health-Related Quality of Life Scores at Week 28



Abbreviations: CI=confidence interval; CFB=change from baseline; DD=dialysis-dependent; LS=least square; SF-36=36-item short form survey.

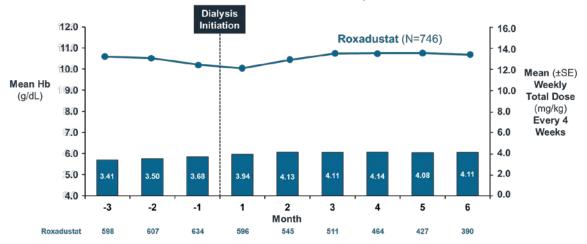
*P-value not controlled for multiplicity.

Note: Full analysis set.

1.4.4. Important Subgroups Across the Continuum of Patients with CKD

As patients were followed for up to 4 years, some patients initiated dialysis during the studies. As shown in Figure 23, roxadustat maintained Hb levels while patients transitioned to dialysis through at least 6 months. The figure shows continued maintenance of Hb through the transition to dialysis initiation.

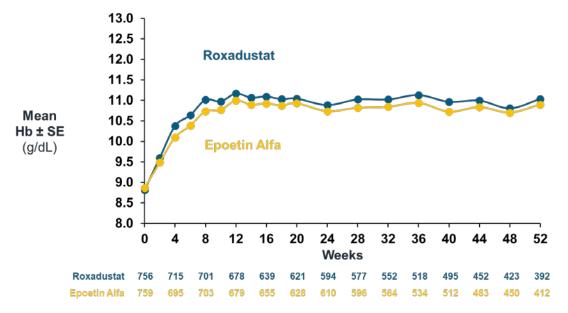
Figure 23: Pooled NDD Studies: Mean Hb and Weekly Roxadustat Dose During the Period of -3 to +6 Months Relative to Chronic Dialysis Initiation



Abbreviations: Hb=hemoglobin; NDD=non-dialysis-dependent; SE=standard error.

For the primary endpoint of mean change in Hb from baseline to the mean over Weeks 28 to 52, roxadustat was non-inferior to EPO in both the ID-DD population (Figure 24) and SDD population (Figure 25).

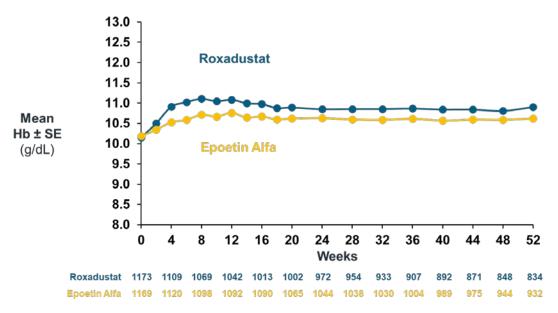
Figure 24: ID-DD Subpopulation: Mean Change in Hb from Baseline to Mean Over Weeks 28 to 52 Regardless of Any Rescue Therapy*



Abbreviations: ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; ID-DD=incident dialysis-dependent; RBC=red blood cell; SE=standard error.

^{*}Rescue therapy consisted of RBC transfusion and ESA.

Figure 25: SDD Subpopulation: Mean Change in Hb from Baseline to Mean Over Weeks 28 to 52 Regardless of Any Rescue Therapy*



Abbreviations: ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; RBC=red blood cells; SDD=stable dialysis-dependent; SE=standard error.

The benefits of roxadustat compared to EPO were also observed across key secondary endpoints in both the ID-DD and SDD populations. Patients in the roxadustat group received a significantly lower monthly amount of IV iron than those in the EPO group (p=0.0001), and a similar number of patients treated with roxadustat and with EPO required RBC transfusions (Table 4).

Table 4: ID-DD and SDD Populations: Mean Monthly IV Iron Use and Red Blood Cell Transfusion Requirement

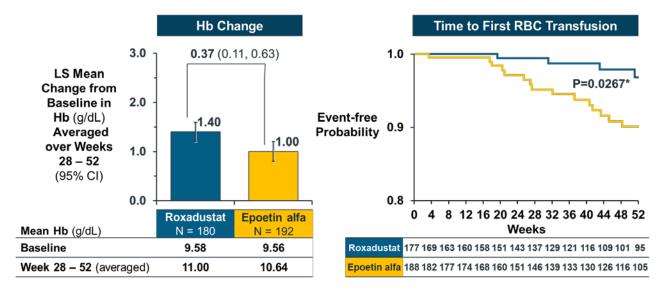
	Incident Dia	lysis (ID-DD)	Stable Dialysis (SDD)	
	Roxadustat Epoetin alfa N=756 N=759		Roxadustat N=1173	Epoetin alfa N=1169
Mean Monthly IV Iron Use over Weeks 28 to 52, mg	53.6	70.2	51.4	64.89
RBC Transfusion; Patients (%)	6.1%	6.7%	11.8%	16.7%

Abbreviations: ID-DD=incident dialysis-dependent; IV=intravenous(ly); RBC=red blood cell; SDD=stable dialysis-dependent.

It is also important to examine the results of roxadustat among the subgroup of patients in the DD studies utilizing peritoneal dialysis as their modality (n=372 [9.6%]). Roxadustat was non-inferior to EPO among patients on peritoneal dialysis in the primary endpoint of change from baseline in Hb (Figure 26). In addition, patients receiving roxadustat received fewer RBC transfusions during the treatment period.

^{*}Rescue therapy consisted of RBC transfusion and ESA.

Figure 26: DD Subpopulation: LSMean Change from Baseline in Hb to Mean Over Weeks 28 to 52 and Time to First RBC Transfusion in Patients Receiving Peritoneal Dialysis



Abbreviations: CI=confidence interval; DD=dialysis-dependent; Hb=hemoglobin; LS=least square; RBC=red blood cell. *P-value not controlled for multiplicity.

Note: A total of 372 patients (9.6% of the enrolled DD population) were on peritoneal dialysis.

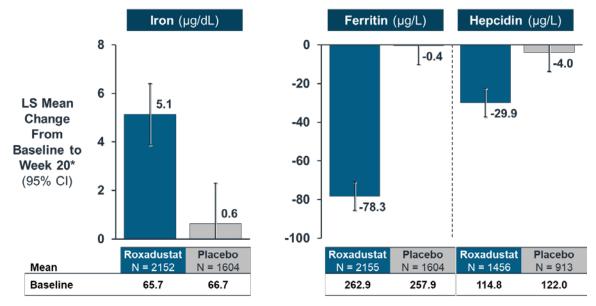
1.5. Hepcidin Reduction and Iron Mobilization

In patients with CKD undergoing ESA therapy, patients with systemic inflammation tend to have decreased response to ESA, requiring higher ESA doses to attempt to achieve target Hb. Whereas no singular definition of hyporesponse exists, studies show that patients have variable responsiveness to ESA longitudinally and 40% of patients enter the highest quintile of ESA dose at some point during a year. Inflammation also results in increased hepcidin and iron sequestration (Ganz 2003). The importance of iron availability is demonstrated in hemodialysis studies where higher ferritin values are achieved as an attempt to overcome iron restricted erythropoiesis and achieve target Hb levels without higher doses of ESAs. Unfortunately, patients with higher ferritin levels have the highest mortality rate (Bradbury et al 2009).

While somewhat similar to absolute iron deficiency, the obvious difference between absolute and functional iron deficiency is that in the latter clinical scenario more than sufficient iron is present in the body. This iron is however sequestered by hepcidin and not available to the organs including the bone marrow that utilize it. A growing number of studies have demonstrated better outcomes among patients with heart failure when iron is repleted using the IV route (Anker et al 2018). A potential outcome of hepcidin reduction is similarly to have a new availability of sufficient iron to organs that need it by decreasing its sequestration.

As shown in Figure 27, roxadustat increased serum iron compared to placebo in patients with NDD CKD. Importantly, this increase in serum iron occurred in the setting of less IV iron use in the roxadustat group compared to placebo likely due to increased absorption from the gastrointestinal tract as well as mobilization from previously sequestered stores. Patients receiving roxadustat also had a reduction in hepcidin and then ferritin. Hepcidin sequesters iron in the body where it cannot be delivered to the bone marrow. These findings support that roxadustat reduces hepcidin and increases iron availability to the bone marrow (as demonstrated by increasing serum iron and reduced ferritin).

Figure 27: Pooled NDD Studies: LSMean Change from Baseline to Week 20 in Iron, Ferritin, and Hepcidin Levels



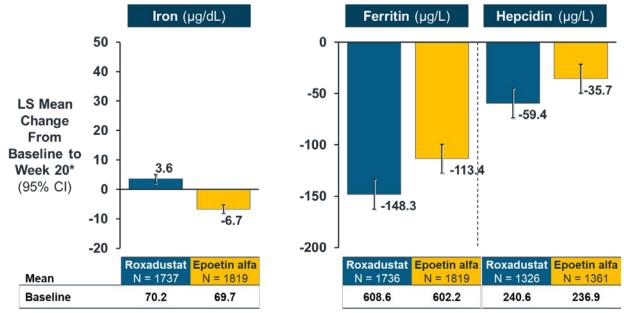
Abbreviations: CI=confidence interval; NDD=non-dialysis-dependent; LS=least square.

*Week 20=the mean of Weeks 12-28; hepcidin data are mean change from baseline to Week 24.

Note: Full analysis set.

Similar results were seen in the DD population (Figure 28). While serum iron was decreased in patients receiving EPO, serum iron was increased in the roxadustat group, despite less IV iron administration, lower rates of transfusion, and slightly higher Hb levels. As seen in the NDD studies, the increases in iron and reduction in ferritin with roxadustat suggest increased iron mobilization from previously trapped stores.

Figure 28: Pooled DD Studies: LSMean Change from Baseline to Week 20 in Iron, Ferritin, and Hepcidin Levels



Abbreviations: CI=confidence interval; DD=dialysis-dependent; LS=least square.

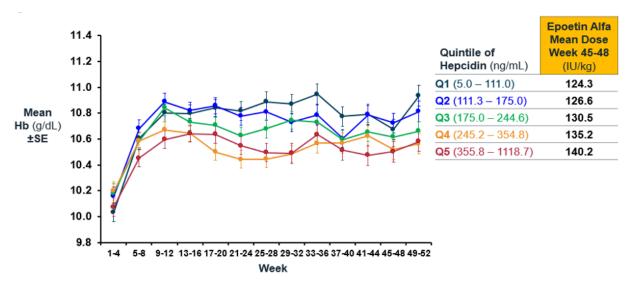
*Week 20=the mean of Weeks 12-28; hepcidin data are mean change from baseline to Week 24.

Note: Full analysis set.

Inflammation is a common occurrence in patients with DD CKD and leads to increased hepcidin levels. In the presence of high hepcidin levels, iron stores are less accessible to be transported by the blood to the bone marrow. Under normal conditions, serum ferritin levels correlate with total body stores of iron. In the presence of inflammation, iron is sequestered in intracellular stores such as macrophages and the reticuloendothelial system, resulting in functional iron deficiency. The treatment of anemia in patients with functional iron deficiency requires the mobilization of this sequestered iron for it to be accessible by the bone marrow (Macdougall et al 1992).

When examined by baseline quintiles of serum hepcidin, the Hb curves appeared to be clinically dissimilar among patients treated with EPO (Figure 29). Among patients with DD CKD treated with EPO, Hb levels in the patients in the 2 greatest hepcidin quintiles did not reach the same Hb levels as in the patients in the lower 3 hepcidin quintiles, despite higher EPO doses.

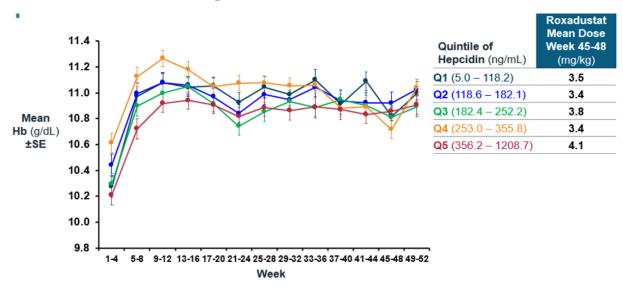
Figure 29: Pooled DD Studies: Mean Hb Levels by Quintiles of Hepcidin at Baseline in the Epoetin Alfa Group



Abbreviations: DD=dialysis-dependent; Hb=hemoglobin; SE=standard error.

However, in patients with DD CKD treated with roxadustat, the Hb levels achieved with were more similar across hepcidin quintiles (Figure 30). The data support that roxadustat efficacy was maintained across levels of hepcidin, whereas the efficacy of EPO was attenuated at the highest hepcidin levels.

Figure 30: Pooled DD Studies: Mean Hb Levels by Quintiles of Hepcidin at Baseline in the Roxadustat Group



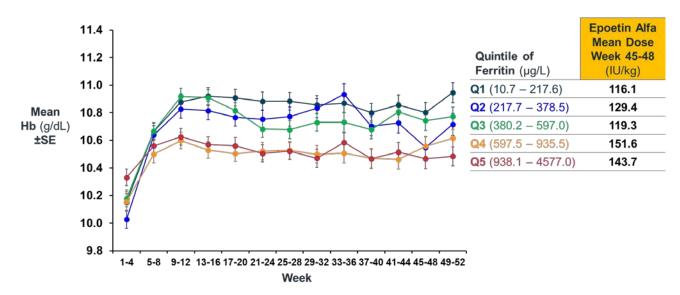
Abbreviations: DD=dialysis-dependent; Hb=hemoglobin; SE=standard error.

While the mean Hb among quintiles was approximately 0.5 g/dL lower among patients with DD CKD treated with EPO in the groups with the highest hepcidin levels, it must be emphasized that one of the central goals of anemia treatment is to minimize or avoid transfusion. Therefore, the impact of this difference in Hb must be examined relative to its association with transfusion risk.

Among patients with DD CKD who had the highest baseline levels of hepcidin, days with transfusions were reduced in the roxadustat vs EPO-treated patients: 11.6 per 100 PEY vs 21.3 per 100 PEY, respectively. As previously shown, hepcidin levels decreased among patients taking roxadustat. Consequently, there was more iron available making roxadustat a more effective treatment of anemia in these patients.

Similar relationships were seen when quintiles of ferritin at baseline were examined. Serum ferritin levels reflect intracellular stores of iron. In addition, in inflammation ferritin can be elevated as an acute phase reactant and can therefore be used as a marker of inflammation similar to CRP. An elevation in serum ferritin in the presence of anemia can suggest the presence of a functional iron deficiency. Similar to the stratification of Hb levels by hepcidin quintiles, patients with DD CKD treated with EPO in the highest 2 quintiles of ferritin at baseline had the lowest Hb levels over time (Figure 31), despite being treated with the highest EPO doses.

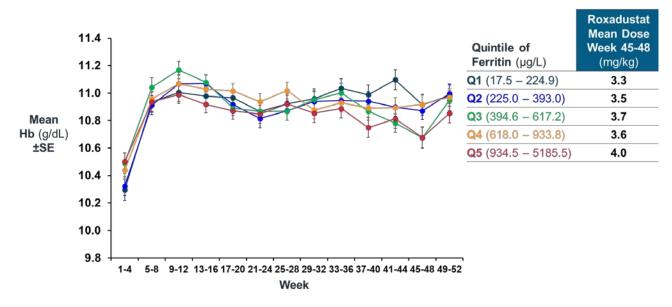
Figure 31: Pooled DD Studies: Mean Hb Levels by Quintiles of Ferritin at Baseline in the Epoetin Alfa Group



Abbreviations: DD=dialysis-dependent; Hb=hemoglobin; SE=standard error.

Similar to stratification of Hb levels by hepcidin quintiles, Hb levels in patients with DD CKD treated with roxadustat were similar across quintiles of ferritin (Figure 32).

Figure 32: Pooled DD Studies: Mean Hb Levels by Quintiles of Ferritin at Baseline in the Roxadustat Group



Abbreviations: DD=dialysis-dependent; Hb=hemoglobin; SE=standard error.

While the difference between the Hb values among patients in the various quintiles of serum ferritin were roughly 0.5 g/dL, the clinical significance of this difference is apparent in the association between these different Hb levels and risk of transfusion.

Among patients with DD CKD who had the highest baseline levels of ferritin, days with transfusions were reduced in the roxadustat vs EPO-treated patients: 12.5 per 100 PEY vs 21.5 per 100 PEY, respectively. This decrease is likely due to the availability of previously sequestered iron stores by reduction of functional iron deficiency.

Inflammation is a significant contributor to the etiology of anemia of CKD. Higher levels of systemic inflammation can contribute to worse and potentially more "treatment-resistant" anemia. Hyporesponsiveness has no single definition in the clinical nephrology community. However, it is characterized by a persistently low Hb level below the desired clinical goal. The roxadustat Phase 3 trials demonstrate the critical role that iron sequestration and functional iron deficiency caused by inflammation plays in the clinical scenario of hyporesponsiveness. Both hepcidin and high ferritin levels are markers of this phenomenon. Hepcidin is likely the mediator of iron sequestration and ferritin is the marker of the iron being sequestered. Patients who have the highest values of both do not achieve the same Hb levels when treated with EPO despite higher doses. Roxadustat, in contrast, effectively treats anemia in this hyporesponsive patient population with less requirement for blood transfusions. Consequently, roxadustat will be an important option for this population of patients with DD CKD.

1.6. Safety Findings (NDD and DD Population)

1.6.1. Cardiovascular Safety

The initial roxadustat Phase 3 program was designed to assess the efficacy and safety of roxadustat compared to placebo in NDD and compared to EPO in DD. Following the FDA's recommendation to

use major adverse cardiovascular event (MACE) defined as ACM, myocardial infarction, and stroke as the primary safety endpoint and to power for non-inferiority, Studies 001 and 002 were added. From the outset, Studies 001 and 002 were intended to contribute to a pooled assessment of CV safety and included the most comprehensive follow-up among the pivotal studies, whereas the initial Phase 3 studies were initially designed to demonstrate efficacy and safety without contributing to a pooled assessment of CV safety.

The CV safety of roxadustat was assessed using time to first adjudicated MACE, time to first MACE+ (MACE plus unstable angina requiring hospitalization and congestive heart failure requiring hospitalization) and time to ACM were also assessed, as well as time to CV mortality and the individual components of MACE+. Reported CV events and all deaths were sent to a blinded central Independent Event Review Committee (IERC) for adjudication. CV safety was assessed by pooling the pivotal studies for each population (001, 060, and 608 for NDD; 002, 063, and 064 for DD). The pooled population HR was estimated using the meta-analysis method to combine the HRs from the individual studies.

The program was designed to have sufficient power to ensure an upper bound of the 95% CI of the HR for MACE of < 1.3 for roxadustat compared to placebo in the NDD population and compared to EPO in the DD population. The upper bound of the 95% CI of the HR of 1.3 was chosen based on precedent from peginesatide and based on the consideration that HRs ≥ 1.3 were considered unacceptable in the Normal Hematocrit and CHOIR trials (Besarab et al 1998; Singh et al 2006). Indeed, the size of the roxadustat clinical program allowed for the generation of a large CV safety database, with more than 8,000 patients from 6 pivotal trials and approximately 1,500 total patients with MACE events in the primary analysis sets.

As discussed further below, results for Study 610, an NDD study with an active control, are presented in order to assess the CV safety of roxadustat vs ESA in NDD patients and to assess the CV safety of roxadustat in NDD patients in a clinical trial setting not affected by informative censoring.

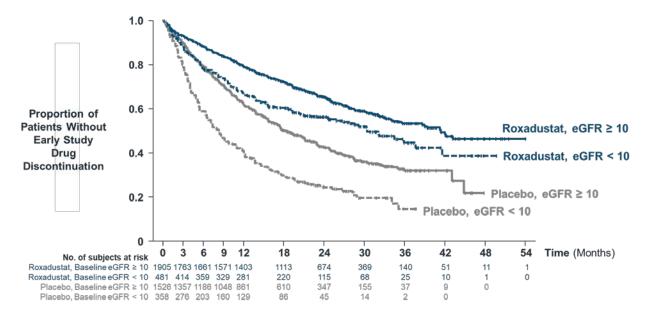
1.6.1.1. NDD Cardiovascular Safety Assessment

As expected, given the intended treatment population of patients with Hb < 10~g/dL, the NDD population consisted largely of patients with severe CKD at baseline. Eighty percent of patients had baseline eGFR < $30~mL/min/1.73~m^2$ (consistent with CKD Stage 4 or 5), and 42% had baseline eGFR < $15~mL/min/1.73~m^2$ (consistent with CKD Stage 5). When assessed by quintiles, the 20% of patients with the lowest baseline eGFR had baseline values < $10~mL/min/1.73~m^2$, which corresponds with the mean eGFR at the time of dialysis initiation in the US (USRDS 2020). As expected, dialysis initiation was common in the Phase 3 NDD program, with 34.7% of patients starting dialysis during the study.

• Placebo was selected as the comparator for the roxadustat NDD program due to the relative infrequency of ESA use in NDD CKD. However, given the severe CKD and high rates of dialysis initiation, many placebo patients required recurrent ESA rescue therapy, leading to large differences in treatment discontinuation between groups (Figure 33) with HR (95% CI) for early treatment discontinuation for roxadustat vs placebo of 0.49 (0.45–0.54). Although rates of discontinuation of placebo were consistently higher compared to roxadustat across subgroups, it was noted that differences were larger among patients with severe CKD, with placebo patients with baseline eGFR < 10 mL/min/1.73 m² being nearly 2.5-times as likely to discontinue treatment early compared to corresponding roxadustat-treated patients (HR for early treatment discontinuation of roxadustat compared to placebo 0.41, 95% CI: 0.34–0.50).

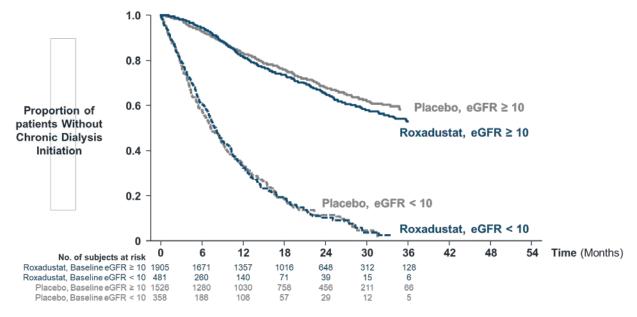
Figure 33 demonstrates this by showing the proportion of patients without early treatment discontinuation over time, including the patients with the lowest baseline eGFR $(< 10 \text{ mL/min/1.73 m}^2)$ and those with baseline values $\ge 10 \text{ mL/min/1.73 m}^2$. Because baseline eGFR < 10 mL/min/1.73 m² was associated with increased risk for MACE regardless of treatment group (HR compared to baseline eGFR ≥ 10: 1.44, 95% CI: 1.22–1.69), these findings have important implications for the CV safety assessment of roxadustat compared to placebo by demonstrating that high-risk patients were retained in the roxadustat group in ontreatment analyses but more likely to be censored from on-treatment analyses in the placebo group. These findings were also noted among patients with more severe anemia, as patients with baseline Hb of < 9 g/dL were much less likely to discontinue roxadustat- treatment early (HR 0.45, 95% CI: 0.39–0.52) and had higher MACE risk regardless of treatment group (HR compared to baseline Hb \geq 9 g/dL 1.47, 95% CI: 1.28–1.69) (Figure 34). In addition to the above, dialysis initiation was an important source of informative censoring (HR, 95% CI for early treatment discontinuation of roxadustat compared to placebo following dialysis initiation was 0.38, 0.32–0.46). As shown in Figure 34, dialysis initiation was common overall, particularly among patients with the lowest quintile of baseline eGFR.

Figure 33: Pooled NDD Studies: Proportion of Patients Without Early Study Drug Discontinuation over Time, by Treatment Group and Baseline eGFR



Abbreviations: eGFR=estimated glomerular filtration rate; NDD-non-dialysis-dependent Note: Safety Population, NDD Pool: Studies 001, 060, 608

Figure 34: Pooled NDD Studies: Proportion of Patients Without Dialysis Initiation over Time, by Treatment Group and Baseline eGFR

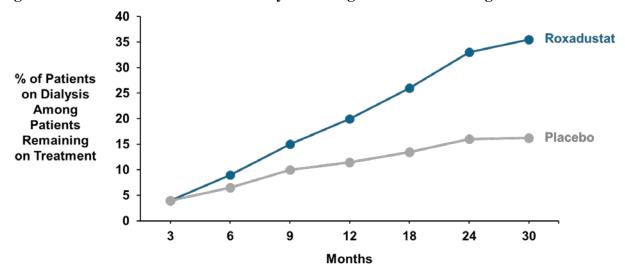


Abbreviations: eGFR=estimated glomerular filtration rate; NDD-non-dialysis-dependent.

Note: Safety Population, NDD Pool: Studies 001, 060, 608

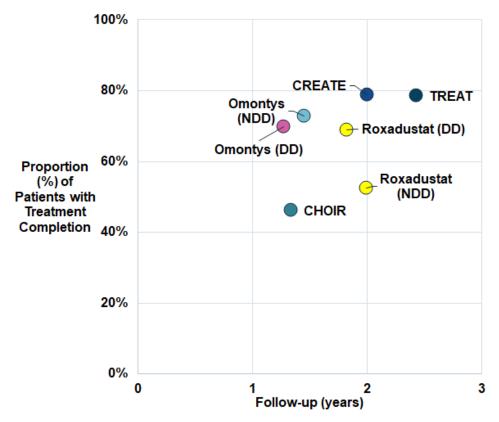
Cumulatively, these findings led to informative censoring of the highest CV risk placebo patients, with fewer high CV risk placebo patients remaining on treatment over time, leading to bias in favor of placebo. For example, over time, a substantially higher proportion of patients remaining on roxadustat treatment were patients who had initiated dialysis (Figure 35) due to placebo patients starting dialysis requiring ESA rescue therapy, compared to roxadustat patients generally having stable Hb values despite dialysis initiation. Because dialysis patients are at substantially higher risk for CV and other events including death, this is another important source of bias in on-treatment analysis. To address these biases, the Sponsor and FDA agreed to preferentially analyze NDD safety data using on-study analysis (also referred to as ITT analyses, including all MACE events accrued during the study, regardless of whether patients remained on treatment at the time of the event).

Figure 35: Percent of Patients on Dialysis Among Patients Remaining on Treatment



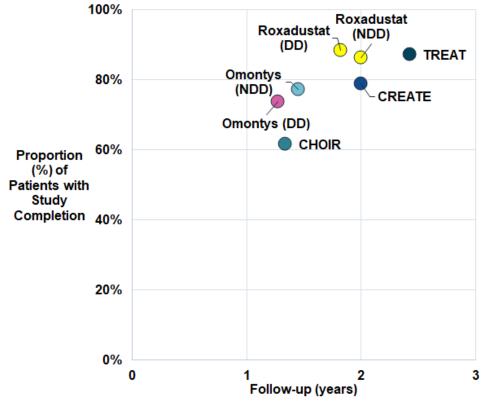
The approach to follow-up of MACE events and vital status after treatment discontinuation varied among the clinical trials. In Study 608, patients that discontinued treatment prematurely were assessed every 6 months until the end of the study for vital status, SAEs, and CV and thromboembolic events, unless consent was withdrawn. Study 060 conducted telephone visits every 3–6 months to assess for CV events, and Study 001 continued study visits with no change to safety data collection but allowed for modified follow-up such as telephone visits when necessary to avoid withdrawal of consent. The by-study and overall percentage of patients with treatment completion and complete follow-up for MACE and mortality are shown in Figure 38. Reasons for treatment discontinuation are presented in Table 59 in Section 10; patient decision was the most common reason for treatment discontinuation. Long-term follow-up of patients was more difficult than in other populations due to the patients' medical complexity and the high proportion of patients who started dialysis. These challenges have been observed with prior CKD anemia trials in both the NDD and DD populations, as shown in Figure 36 and Figure 37. Although the rates of treatment discontinuation in the roxadustat NDD pool were higher than most prior CKD anemia trials, it should be noted that the roxadustat NDD program differed from prior trials by enrolling a patient population with much more severe CKD who required dialysis initiation at higher rates; the rates of study discontinuation in the roxadustat NDD program were lower than most prior CKD anemia programs. Overall, 87.8% and 91.4% of patients had complete follow-up for MACE and vital status, respectively. Among the pivotal NDD trials, follow-up was most complete for Study 001 (Table 36 in Section 6.4.1).

Figure 36: Treatment Completion Rate in Roxadustat and Historical Anemia of CKD Trials



Abbreviations: CHOIR=Correction of Hemoglobin and Outcomes in Renal Insufficiency trial; CKD=chronic kidney disease; CREATE=Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta; DD=dialysis-dependent; NDD=non-dialysis-dependent; TREAT=Trial to Reduce Cardiovascular Events with Aranesp Therapy. Source: Wanner et al 2005; Fellström et al 2009; Singh et al 2006; Drücke et al 2006; Fishbane et al 2013; Evolve Trial Investigators 2012; Macdougall et al 2013; Macdougall et al 2019; Pfeffer et al 2009.

Figure 37: Study Completion Rate in Roxadustat and Historical Anemia of CKD Trials



Abbreviations: CHOIR=Correction of Hemoglobin and Outcomes in Renal Insufficiency trial; CKD=chronic kidney disease; CREATE=Cardiovascular Risk Reduction by Early Anemia Treatment with Epoetin Beta; DD=dialysis-dependent; NDD=non-dialysis-dependent; TREAT=Trial to Reduce Cardiovascular Events with Aranesp Therapy. Source: Wanner et al 2005; Fellström et al 2009; Singh et al 2006; Drüeke et al 2006; Fishbane et al 2013; Evolve Trial Investigators 2012; Macdougall et al 2013; Macdougall et al 2019; Pfeffer et al 2009.

Another way to assess follow-up is to evaluate mean follow-up time on treatment, mean follow-up time for MACE, and mean follow-up time for ACM. Table 5 shows these analyses by treatment group overall and Table 6 shows by treatment group and baseline eGFR. As expected, follow-up time ontreatment was substantially longer for roxadustat compared to placebo; however, follow-up time for MACE and ACM was comparable by treatment group. Ninety percent of MACE follow-up for roxadustat occurred during the OT+28 period, compared to 72% for placebo. This difference suggests that any amount of incomplete ascertainment of CV safety data following the on-treatment-period would be expected to lead to bias in favor of placebo in the ITT/on-study analysis, and that additional analyses which include a more balanced proportion of observation time occurring on treatment could further reduce bias due to differential treatment discontinuation. On review of the data by baseline eGFR, it is noted that the proportion of overall on-study/ITT follow-up that occurred during the ontreatment period is more consistent in the roxadustat group, and that follow-up time on treatment (and proportion of on-study/ITT follow-up time which occurred on-treatment) was particularly low among placebo patients with baseline eGFR < 10 mL/min/1.73 m². In sum, this analysis confirms the potential for informative censoring and bias favoring the placebo group in the OT+28 period, which will be attenuated in the ITT/on-study analysis.

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The overall on-study analysis includes time when patients from both treatment groups were on dialysis and time when a high proportion of placebo patients had converted to ESA. In order to focus on the clinical question of the CV safety of roxadustat compared to placebo in patients not on dialysis, "NDD-NDD" results are presented, which censor at dialysis initiation for patients who initiated dialysis during the study. It is acknowledged that this analysis has limitations due to censoring at a post-randomization event. Additionally, on-study results for patients with baseline eGFR ≥ 10 mL/min/1.73 m² are presented as supportive analyses to focus on the 80% of patients most likely to remain dialysis independent and who are less affected by differences in treatment discontinuation. As shown in Table 6, differences in on-treatment vs off-treatment follow-up time were less pronounced in this subgroup. Finally, results from Study 001 are shown as well as the pooled results because this study had the most complete follow-up for CV safety and mortality events.

Table 5: Mean Follow-up Time in Years, in On-treatment Plus 28 Days (OT+28) Analysis Set for MACE and ACM

	Follow-up Time/Patient, Roxadustat			Follow-up Time/Patient, Placebo		
	OT-28	MACE	ACM	OT-28	MACE	ACM
Pooled	1.7	1.9	2.0	1.3	1.8	2.0
Percent of overall follow-up time during OT+28 period		90%	84%		72%	66%

Abbreviations: ACM=all-cause mortality, MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke)

Table 6: Mean Follow-Up Time in Years, in the On-treatment Plus 28 Days Analysis Set for MACE and ACM by Baseline eGFR

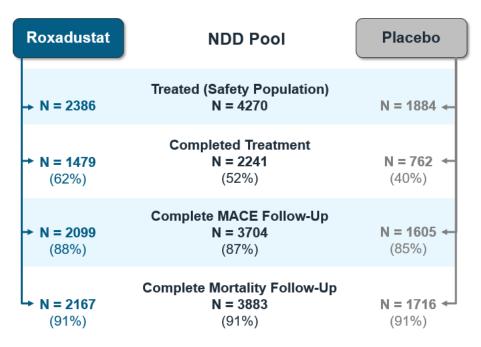
	Follow-up	Follow-up Time/Patient, Roxadustat			Follow-up Time/Patient, Placebo		
	OT+28	MACE	ACM	OT+28	MACE	ACM	
eGFR < 10*	1.5	1.7	1.8	1.0	1.7	1.9	
Percent of overall follow-up time during OT+28 period		85%	79%		57%	51%	
eGFR < 10 - < 20*	1.7	2.0	2.1	1.2	1.8	1.9	
Percent of overall follow-up time during OT+28 period		89%	83%		70%	64%	
eGFR 20 - < 30*	1.8	1.9	2.0	1.5	1.9	2.1	
Percent of overall follow-up time during OT+28 period		92%	88%		79%	72%	
eGFR≥30*	1.8	1.9	2.0	1.6	1.9	2.0	
Percent of overall follow-up time during OT+28 period		93%	87%		82%	77%	

Abbreviations: ACM=all-cause mortality; eGFR=estimated glomerular filtration rate; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); OT+28=on-treatment plus 28 days. * $mL/min/1.73\ m^2$

1.6.1.1.1. NDD Cardiovascular Safety Results

Figure 38 shows treatment discontinuation and ascertainment of MACE and ACM for the pooled NDD population. Sixty-two percent of roxadustat patients completed treatment compared to 40% of placebo patients, and a similar proportion of patients in each group had complete follow--up for MACE and ACM.

Figure 38: Pooled NDD Studies: Retention and Follow-up



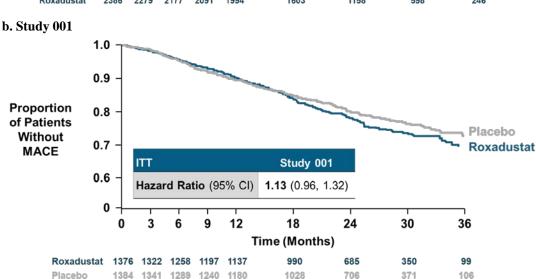
Abbreviation: NDD=non-dialysis-dependent.

The Kaplan-Meier survival analysis plots for the endpoint of MACE shows the probability of remaining event-free over time for the pooled NDD program and for the largest study in the program (Study 001), which had the most comprehensive follow-up of CV safety. The HR (95% CI) for MACE for roxadustat compared to placebo was 1.10 (0.96–1.27), in the pooled NDD assessment, and the results for Study 001 were consistent with the pooled results (Figure 39).

a. Pooled NDD Studies

Figure 39: Pooled NDD Studies: Kaplan-Meier Curves of Primary Analysis of MACE

0.9 Placebo Proportion 8.0 of Patients Without MACE 0.7 Roxadustat MACE NDD Pool 0.6 Hazard Ratio (95% CI) 1.10 (0.96, 1.27) 0.0 36 18 30 0 12 24 Time (months) 1237 1884 1802 1686 1596 1508 851 428 142 2386 2279 1994 1603 1158 598 246



Abbreviations: CI=confidence interval; ITT=intent-to-treat analysis set; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); NDD=non-dialysis-dependent.

Note: Safety Population; On-study analysis, NDD Pool: Studies 001, 060, 608, hazard ratio upper bound of 95% CI below reference margin of 1.3.

Figure 40 shows risk for MACE, MACE +, and ACM for roxadustat compared to placebo. HR point estimates range from 1.07–1.10, with 95% CIs crossing 1.0 and with 95% CI upper bounds ranging from 1.21–1.27 (Figure 40, top panel). When the data are censored at dialysis initiation (NDD-NDD), HR point estimates were nearly 1.0 (Figure 40, middle panel) and 95% CI upper bounds ranged from 1.19–1.21. This analysis includes 568 patients with MACE events and is considered important for assessing the CV safety of roxadustat for patients not on dialysis. Upon evaluation of the approximately 80% of total patients with baseline eGFR \geq 10 mL/min/1.73 m², who were less affected by differences in treatment discontinuation and who were less likely to start dialysis during the program, HR point estimates were also close to 1.0 (Figure 40, bottom panel).

Figure 40: Pooled NDD Studies: Forest Plot of Primary Analysis of MACE, MACE+, and ACM

a. Pooled NDD Studies

NDD Pool	Roxadustat N = 2386	Placebo N = 1884	Favors Roxadustat	Hazard Ratio (95% CI)
MACE	480 (20.1%)	350 (18.6%)	——	1.10 (0.96, 1.27)
MACE +	578 (24.2%)	432 (22.9%)	—	1.07 (0.94, 1.21)
ACM	400 (16.8%)	301 (16.0%)		1.08 (0.93, 1.26)
		0.	5 1	2

b. NDD-NDD

Pooled NDD-NDD	Roxadustat N = 2386	Placebo N = 1884	Favors Roxadustat	Hazard Ratio (95% CI)
MACE	313 (13.1%)	255 (13.5%)	⊢	1.02 (0.86, 1.21)
MACE+	407 (17.1%)	324 (17.2%)	⊢	1.03 (0.89, 1.19)
ACM	251 (10.5%)	213 (11.3%)	—	1.00 (0.83, 1.21)
		0	5 1	

c. eGFR \geq 10 mL/min/1.73 m²

	Roxadustat N = 1905	Placebo N = 1526	Favors Roxadustat	Hazard Ratio (95% CI)		
MACE	351 (18.4%)	276 (18.1%)		1.00 (0.85, 1.17)		
MACE+	428 (22.5%)	334 (21.9%)	—	0.99 (0.86, 1.15)		
ACM	287 (15.1%)	236 (15.5%)	·	0.96 (0.81, 1.15)		
0.5 1 2						

Abbreviations: ACM=all-cause mortality; CI=confidence interval; eGFR=estimated glomerular filtration rate; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=m MACE, plus hospitalization for unstable angina or congestive heart failure; NDD=non-dialysis-dependent. Note: Safety Population; On-study analysis (Studies 001, 060, 608; N=4,270); hazard ratio upper bound of 95% CI below reference margin of 1.3.

Results for Study 001 were consistent with the pooled results, for on-study NDD, on-study NDD with censoring at dialysis initiation, and on-study NDD with baseline eGFR \geq 10 mL/min/1.73 m² (Table 38).

The NDD program was not powered for the comparison of CV mortality or MACE+ components for roxadustat and placebo, and in particular there were relatively few myocardial infarction and stroke events during the program. HR point estimates varied by endpoint, however 95% CIs crossed 1.0 for all endpoints (Table 7).

Table 7: Pooled NDD Studies: Cardiovascular Mortality and MACE+ Components

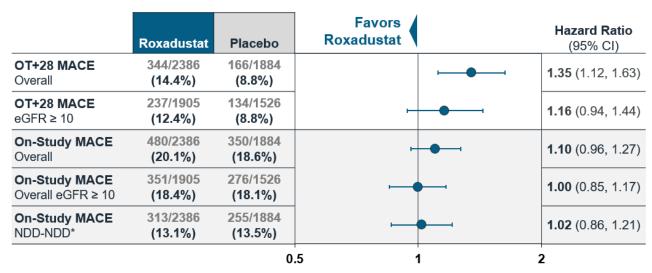
	Roxadustat N=2386	Placebo N=1884	HR (95% CI)
Event	n (%)	n (%)	
Death (all-cause mortality)	400 (16.8%)	301 (16.0%)	1.08 (0.93, 1.26)
Cardiovascular-related mortality	143 (6.0%)	102 (5.4%)	1.11 (0.86, 1.44)
Myocardial infarction	86 (3.6%)	52 (2.8%)	1.29 (0.90, 1.85)
Stroke	56 (2.3%)	36 (1.9%)	1.25 (0.82, 1.90)
Hospitalization for Unstable angina	15 (0.6%)	12 (0.6%)	0.56 (0.22, 1.42)
Hospitalization for Congestive heart failure	175 (7.3%)	151 (8.0%)	0.93 (0.75, 1.16)

 $Abbreviations: CI=confidence\ interval;\ HR=hazard\ ratio;\ NDD=non-dialysis-dependent.$

Note: Safety Population; On-study analysis (Studies 001, 060, 608; N=4270)

Figure 41 shows MACE results presented above, as well as overall on-treatment MACE and on-treatment MACE in patients with baseline eGFR ≥ 10 mL/min/1.73 m². The on-treatment analyses are heavily influenced by bias due to informative censoring in the placebo group and are not considered representative of the CV safety profile of roxadustat. The overall on-study/ITT HR for MACE was 1.10. On-study analyses with censoring at dialysis initiation, and of the subgroup of patients with baseline eGFR of ≥ 10 mL/min/1.73 m² were less affected by differential treatment discontinuation and had MACE HR point estimates of 1.02 and 1.00, respectively.

Figure 41: Pooled NDD Studies: Results for MACE Vary Due to Impact of Differential Treatment Discontinuation



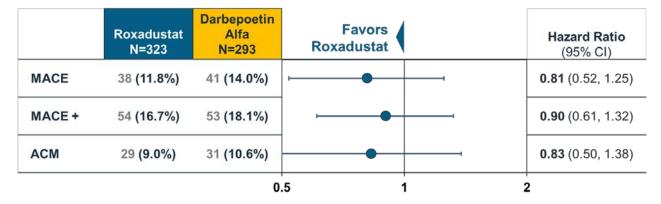
 $Abbreviations: eGFR = estimated \ glomerular \ filtration \ rate; \ MACE = major \ adverse \ cardiovascular \ event \ (all-cause \ mortality, \ myocardial \ infarction, \ and \ stroke); \ NDD = non-dialysis-dependent.$

Note: Safety Population; OT+28 analysis or On-study analysis (Studies 001, 060, 608; N=4270)

Although ESAs are used infrequently in NDD CKD anemia, they are approved for use in the US, and the placebo-controlled NDD program does not directly address the question of the CV safety of roxadustat compared to ESAs in this population. Study 610 is considered informative due to its unique

design as an active-controlled (darbepoetin alfa) NDD study which is not affected by substantial differences in study drug discontinuation and informative censoring. The CV safety results for 610 showed MACE, MACE+, and ACM with HR point estimates ranging from 0.81–0.90 (Figure 42).

Figure 42: Study 610: Forest Plot of Primary Analysis of MACE, MACE+, and ACM



Abbreviations: ACM=all-cause mortality; CI=confidence interval; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days. Note: Safety Population, OT+28 analysis.

1.6.1.2. DD Cardiovascular Safety Assessment

In agreement with FDA, the pooled CV safety assessment of roxadustat in patients with DD CKD anemia is based on Studies 063, 064, and 002. Each of these studies compared open-label roxadustat to open-label EPO. The Phase 3 study, Study 613, had a different design and is assessed separately.

The DD population consisted of patients from Studies 063, 064, and 002. Study 063 was a study of ID patients randomized within 4 months following dialysis initiation. These patients were untreated with ESA at baseline, had low Hb levels, and required anemia correction followed by maintenance. Study 064 was a study of prevalent dialysis (mean 3.9 years) patients treated with stable doses of ESA at baseline, and with Hb values of 9–12 g/dL. These patients were randomized to either continued maintenance anemia treatment with ESA, or conversion to roxadustat followed by titration and maintenance. Study 002 was the largest study in the program and contained a mix of incident and prevalent dialysis patients, and a mix of patients treated and untreated with ESA at baseline.

The ID subpopulation is considered to be a clinically relevant population because anemia treatment is most commonly initiated in conjunction with dialysis initiation, and because these patients were generally untreated with ESA at baseline or had recently been initiated on ESA. By contrast, most prevalent—or stable—dialysis patients had been on ESA treatment long-term, and these patients commonly had baseline Hb values within target ranges on low doses of ESA. The population of stable dialysis patients studied in the roxadustat program thus represents a population where transition to a different anemia therapy may not be clinically warranted for many patients. Therefore, the Sponsor considers that incident dialysis data are important for the assessment of the cardiovascular safety of roxadustat in patients with DD CKD.

1.6.1.2.1. DD Cardiovascular Safety Results

Figure 43 shows treatment discontinuation and ascertainment of MACE and ACM for the pooled DD population. Sixty-six percent of EPO-treated patients completed treatment compared to 58% of roxadustat-treated patients, and a similar proportion of patients by treatment group had complete follow-up for MACE and ACM. Reasons for treatment discontinuation, and treatment discontinuation in the ID and SDD subpopulations are presented in Table 60 in Section 10. Treatment discontinuation was more balanced by treatment group in the ID compared to the SDD subgroup. "Withdrawal by patient" was the most common reason for treatment discontinuation. As shown in Figure 36 and Figure 37, the incidence of early treatment discontinuation was comparable to prior large NDD and DD CKD anemia trials, and the rates of study discontinuation were generally lower in the roxadustat DD CKD program.

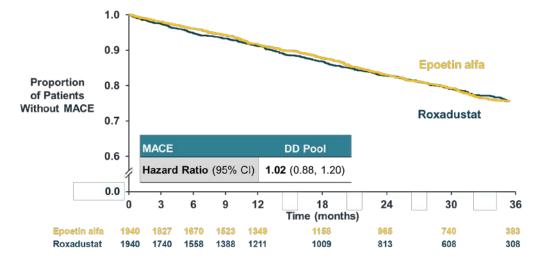
Figure 43: Pooled DD Studies: Retention and Follow-up

Roxadustat	NDD Pool	Epoetin Alfa
→ N = 1940	Treated (Safety Population) N = 3880	N = 1940 ←
→ N = 1130 (58%)	Completed Treatment N = 2417 (62%)	N = 1287 ← (66%)
→ N = 1719 (89%)	Complete MACE Follow-Up N = 3458 (89%)	N = 1739 ← (90%)
→ N = 1762 (91%)	Complete Mortality Follow-Up N = 3547 (91%)	N = 1785 ← (92%)

Abbreviation: DD=dialysis-dependent.

The Kaplan-Meier survival analysis plot for the endpoint of MACE shows the survival curves of the 2 groups tracking closely (Figure 44). Results for additional analysis sets are provided in Section 6.4.2.

Figure 44: Pooled DD Studies: Kaplan-Meier Curves of Primary Analysis of MACE

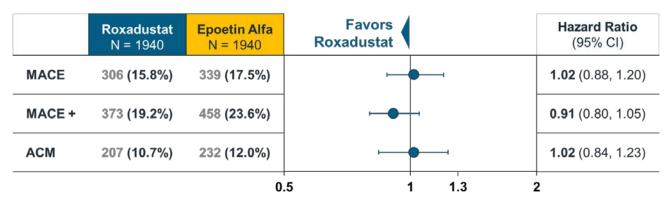


Abbreviations: CI=confidence interval; DD=dialysis-dependent; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); OT+7=on-treatment plus 7 days.

Note: Safety Population; OT+7 analysis (Studies 002, 063, 064, N=3880).

CV safety findings in the DD population were comparable between roxadustat and EPO. The forest plot presenting primary analysis of MACE, MACE+, and ACM shows HR point estimates ranging from 0.91–1.02, with 95% CIs crossing 1.0 and 95% CI upper bounds of 1.05–1.23 (Figure 45). Additional CV safety results in the DD population are presented in Section 6.4.2.

Figure 45: Pooled DD Studies: Forest Plot of Primary Analysis of MACE, MACE+, and ACM



Abbreviations: ACM=all-cause mortality; CI=confidence interval; DD=dialysis-dependent; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure

Note: Safety Population; OT+7 analysis (Studies 002, 063, 064, N=3880)

Incidence rates of MACE+ individual components were generally similar for roxadustat and EPO, and numerically lower for hospitalization for congestive heart failure in roxadustat-treated patients (Table 8).

Tuble of Toolea DD Staalest Mile D1 Components	Table 8:	Pooled DD Studies: MACE+ Components
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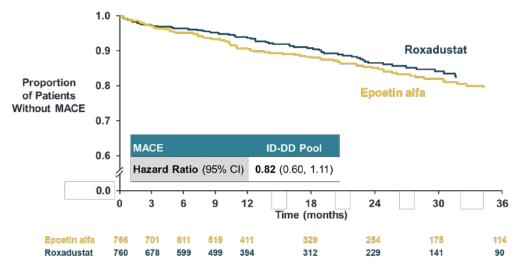
	Roxadustat N=1940	Epoetin Alfa N=1940	
MACE+ Components	n (%)	n (%)	HR (95% CI)
All-Cause Mortality	207 (10.7%)	232 (12.0%)	1.02 (0.84, 1.23)
Cardiovascular-Related Mortality	122 (6.3%)	136 (7.0%)	1.02 (0.80, 1.31)
Myocardial infarction	103 (5.3%)	109 (5.6%)	1.07 (0.82, 1.40)
Stroke	45 (2.3%)	50 (2.6%)	1.04 (0.69, 1.56)
Unstable angina	18 (0.9%)	22 (1.1%)	0.89 (0.48, 1.67)
Congestive heart failure	120 (6.2%)	166 (8.6%)	0.83 (0.66, 1.05)

Abbreviations: CI=confidence interval; DD=dialysis-dependent; HR=hazard ratio; MACE+=major adverse cardiovascular event including hospitalizations for either unstable angina and/or congestive heart failure; OT+7=on-treatment plus 7 days.

Note: Safety Population; OT+7 analyses (Studies 002, 063, 064, N=3880)

To further evaluate the results in patients with ID and SDD CKD, pooled analyses were performed. It should be noted that these analyses were not powered for non-inferiority. Figure 46 shows the proportion of ID patients without MACE over time for roxadustat compared to EPO. Although the 95% CI crossed 1.0, the curves for the proportion of patients without MACE appeared to separate over time, and the HR point estimate for MACE was 0.82 for roxadustat compared to EPO.

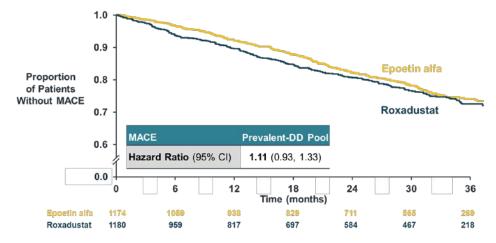
Figure 46: ID-DD Subpopulation: Kaplan-Meier Curve of Primary Analysis of MACE



Abbreviations: CI=confidence interval; ID-DD=incident dialysis dialysis-dependent; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); OT+7=on-treatment plus 7 days. Note: Safety Population; OT+7 analyses (Studies 002, 063, 064, N=1526 for patients on dialysis for \leq 4 months at the time of randomization)

The Kaplan-Meier survival analysis plot for MACE shows similar curves in MACE for roxadustat and EPO in SDD or prevalent dialysis patients (Figure 47). The HR point estimate was 1.11, with a 95% CI crossing 1.0.

Figure 47: SDD-DD Subpopulation: Kaplan-Meier Curve of Primary Analysis of MACE



Abbreviations: CI=confidence interval; SDD=stable dialysis-dependent; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); OT+7=on-treatment plus 7 days.

Note: Safety Population; OT+7 analyses (Studies 002, 063, 064, N=2354 for patients on dialysis for > 4 months at the time of randomization).

1.6.1.3. Analysis of Pooled DD Studies With and Without Study 613

Figure 48 shows CV safety results for the pooled DD studies with and without Study 613. Study 613 was a study of stable dialysis patients on ESA at baseline. Patients on short-acting ESAs were randomized to roxadustat or EPO, whereas patients on long-acting ESA were randomized to roxadustat or darbepoetin. In agreement with FDA, Study 613 was not pooled with the other 3 Phase 3 trials for the NDA because it randomized to roxadustat and 2 different ESAs, which may have different profiles. The results for Study 613 are shown in Figure 71, and the pooled DD analysis including Study 613 is presented below.

Favors DD Pool Excludes Roxa **EPO Hazard Ratio** N=1940 Roxadustat Study 613 N = 1940(95% CI) MACE 306 (15.8%) 339 (17.5%) **1.02** (0.88, 1.20) MACE+ 373 (19.2%) 458 (23.6%) **0.91** (0.80, 1.05) **All-Cause Mortality** 207 (10.7%) 232 (12.0%) **1.02** (0.84, 1.23) **DD Pool Includes** Roxa **ESA Hazard Ratio** Study 613 N=2354 N=2360 (95% CI) MACE 371 (15.8%) 398 (16.9%) 1.08 (0.93, 1.24) MACE+ 445 (18.9%) 524 (22.2%) 0.97 (0.85, 1.10) **All-Cause Mortality** 264 (11.2%) 277 (11.7%) **1.11** (0.94, 1.32) 0.5 2 1.3

Figure 48: Analysis of Pooled Dialysis Studies With and Without Study 613

Abbreviations: ACM=all-cause mortality; CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure OT+7=on-treatment plus 7 days; Roxa=roxadustat. Note: Safety Population; OT+7 analysis

As expected, based on the effect of including Study 613 in the pooled analysis, Study 613 is an outlier compared to the pivotal DD studies (Figure 49; MACE+ and ACM are shown in Figure 71).

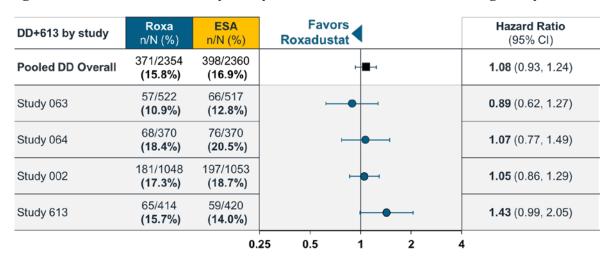


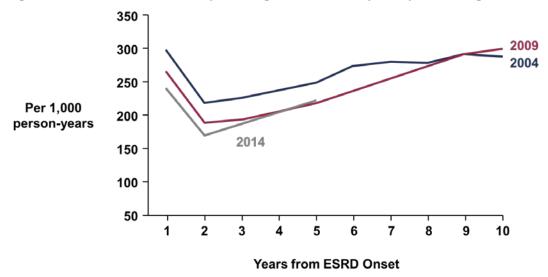
Figure 49: MACE Results by Study for Pivotal DD Studies Including Study 613

Abbreviations: CI=confidence interval; DD=dialysis-dependent; ESA=erythropoietin-stimulating agent; Roxa=roxadustat.

In addition to the differences in trial design as discussed above, analysis of demographic and baseline characteristics showed apparent baseline imbalances by treatment group design in Study 613 (Table 54). Such imbalances were not noted in the pivotal DD studies, and several of the noted imbalances in Study 613 were in baseline characteristics known to be associated with CV risk, suggesting that the treatment groups may not have had balanced CV risk at baseline. Notably, dialysis

vintage (time since initiation of dialysis) differed by treatment group. Dialysis vintage is important prognostically. As shown in Figure 50, there is a "U-shaped" association between mortality and dialysis vintage in US patients, with high mortality rates in the ID period, which decline sharply until ~2 years following randomization, then increasing to rates which approach rates in the ID period by ~5 years following dialysis initiation. These results demonstrate how the observed differences in mean dialysis vintage in Study 613 could lead to confounding in the assessment of CV safety for roxadustat versus the comparators (Table 54).

Figure 50: Rate of Mortality Among US Patients by Dialysis Vintage



Abbreviation: ESRD=end-stage renal disease.

Source: USRDS 2020

1.6.1.4. Cardiovascular Safety Conclusions

The CV safety of roxadustat is comparable to placebo in NDD CKD and to EPO in DD CKD. The CV safety results of the roxadustat NDD program should be interpreted in the context of the use of the placebo comparator. By contrast, prior seminal ESA NDD trials have generally used ESA as comparator, with the notable exception of TREAT, which showed an increased risk of stroke for darbepoetin compared to placebo. Notably, the NDD Study 610 compared roxadustat to darbepoetin alfa.

The CV safety results in the NDD program are affected by informative censoring of placebo patients, with higher-risk patients being more likely to prematurely discontinue placebo than corresponding roxadustat patients who were more likely to continue treatment. The pooled NDD on-study analyses showed HR point estimate of 1.10 with a 95% CI that crossed 1.0, with upper bound of 1.27. Supportive results in patients with baseline eGFR \geq 10 mL/min/1.73 m², and in patients censored at dialysis initiation, which the Sponsor considers to be less affected by informative censoring, showed HR point estimates close to 1.0, with 95% CIs crossing 1.0. In addition, CV safety results of Study 001, which was the largest pivotal NDD study that had the most complete follow-up for CV events after treatment discontinuation, were consistent with the pooled results.

The non-pooled NDD Study 610 that was notable for being active controlled (darbepoetin alfa), rather than placebo controlled, showed MACE, MACE+, and ACM HR point estimates of 0.81, 0.90, 0.83, respectively, with 95% CIs crossing 1.0.

The pooled DD results show comparable CV safety profiles in roxadustat compared to ESA, particularly in the clinically relevant subgroup of ID patients.

1.6.2. Adverse Events

The AE profile of roxadustat was generally comparable to placebo in patients with NDD CKD and to EPO in patients with DD CKD (Table 9), with some exceptions as noted below. Informative censoring also affected the interpretation of AEs in the NDD population. To account for differences in study drug exposure per treatment group in this population, exposure-adjusted incidence rates are presented in addition to incidence. However, this does not account for overrepresentation of higher-risk patients in the roxadustat group for on-treatment analyses. AE profiles and lists of most commonly reported AEs are presented in Section 6.5.

Table 9: NDD and DD Studies: Overview of Adverse Events

		dustat 2386	Placebo N=1884		
NDD Pool	n (%)	IR/100 PY	n (%)	IR/100 PY	
AEs	2132 (89.4)	222.6	1608 (85.4)	211.5	
AEs leading to discontinuation	157 (6.6)	3.9	92 (4.9)	3.8	
SAEs	1308 (54.8)	45.9	845 (44.9)	43.9	
	Roxadustat N=1940		_	in Alfa 1940	
DD Pool	n (%)	n (%)	
AEs	1680 (86.6)		1669	(86.0)	
AEs leading to discontinuation	218 (11.2)		159	(8.2)	
SAEs	1080 (55.7)		1071	(55.2)	

Abbreviations: AE=adverse event; DD=dialysis-dependent; IR=incidence rate; NDD=non-dialysis-dependent; PY=patient year; SAE=serious adverse event.

Note: Safety Population, OT+28 analysis; NDD Pool=Studies 001, 060, 608, DD Pool=Studies 002, 063, 064

1.6.3. Safety Assessment of Specific Adverse Events

The following AEs have been selected because they have either been previously observed as risks with anemia treatment or because safety imbalances were noted in the roxadustat clinical development program.

1.6.3.1. Thrombosis

Across the randomized NDD and DD populations, the types of thrombosis events reported were typical of those observed in the CKD population, with no imbalances in rare or atypical thrombotic events. However, for both the NDD and DD populations, there were higher numbers of vascular access thrombosis (VAT) and deep vein thrombosis (DVT), in the roxadustat groups than the comparator groups.

For both the NDD and DD populations, there were higher numbers of VAT and venous thrombosis events, specifically DVT, in the roxadustat groups than the comparator groups.

Mechanistically, the risk of thrombosis was associated with rapid increases in Hb levels (defined within the roxadustat program as Hb increase > 2 g/dL over a 4-week period) in the clinical program. In the non-clinical program, thrombotic events were associated with excessive erythropoiesis (hematocrits > 68% and Hb > 20 g/dL) in toxicology studies after long-term roxadustat dosing in healthy animals, though they were at higher doses than what were used in the clinical program.

Summaries of VAT and DVT are provided below.

1.6.3.1.1. Vascular Access Thrombosis

In patients with ESRD receiving hemodialysis, thrombosis is a common cause of dysfunction of a vascular access, including arteriovenous fistula (AVF) and arteriovenous graft (AVG).

All VAT-related AEs reported by the investigators were adjudicated by the IERC. Overall, there was a higher number of (positively) adjudicated VAT events in the roxadustat versus comparator groups across the NDD and DD populations. In the NDD pool, the incidence rate of adjudicated VAT events in the roxadustat versus placebo groups was 1.5 patients with events/100 PY vs 0.9 /100 PY in onstudy analyses, respectively, and 1.5 /100 patient years (PY) vs 0.3 /100 PY in OT+28, respectively. However, in the NDD program, patients typically do not have dialysis access at baseline, and patients requiring dialysis were noted to discontinue placebo at higher rates compared to roxadustat. These circumstances make the NDD VAT data difficult to interpret, and hence the interpretation of VAT data from the roxadustat program is focused on the results in the DD population, where the incidence of adjudicated VAT events in the roxadustat versus EPO groups was 13.0% vs 10.5%, respectively (Table 10).

Table 10: NDD and DD Studies: Adjudicated VAT Adverse Events

	Roxadustat N=2386		Placebo N=1884	
NDD Population	n (%)	n (%) IR/100 PY		IR/100 PY
Vascular Access Thrombosis (OT+28)	58 (2.4)	1.5	7 (0.4)	0.3
	Roxadustat N=1940		Epoetin Alfa N=1940	
DD Population	n (%)	n (%)
Vascular Access Thrombosis (OT+28)	252 (13.0)		204 (10.5)	
Baseline arteriovenous fistula	120/794 (15.1)		92/745	5 (12.3)
Baseline arteriovenous graft	30/76 (39.5) 18/70 (25		(25.7)	

Abbreviations: DD=dialysis-dependent; IR=incidence rate; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PY=patient year.

Note: Safety Population, OT+28 analysis; NDD Pool: Studies 001, 060,608; DD Pool: Studies 002, 063, 064

A limitation to the VAT analyses in the DD pool is that vascular access status was not systematically collected at baseline. However, based on their surgical history, 42% of patients in the DD pool had a documented AVF or graft at baseline, including 841 roxadustat-treated patients and 795 EPO-treated patients. When limiting the analysis to patients with a documented AVF at baseline, 15.1% of roxadustat compared to 12.3% of EPO patients had a VAT event, compared to 39.5% and 25.7% of roxadustat and EPO patients, respectively, with documented AVG at baseline.

In patients with VAT, demographics and baseline disease characteristics were similar between treatment groups. In addition, VAT rates across treatment groups were proportionally greater in the subgroup of patients with known risk factors of VAT (eg, history of cardiovascular/cerebrovascular/thromboembolic disease, diabetes, and obesity).

Rates of VAT in the roxadustat group were highest, and the difference between treatment groups was largest, during the first 12 weeks of the study following randomization (Figure 51). The rates of VAT were noted to decrease over time in both treatment groups, but to a proportionally greater extent in roxadustat-treated patients, and differences in event rates were noted to be of a lesser magnitude, at later compared to earlier time points in the study.

Roxadustat **Epoetin Alfa** 20 15 13.6 Incidence 11.3 10.3 of VAT 10 9.0 (IR/100 PEY) 7.8 7.3 6.7 5.3 5 ≤12 >12 - ≤24 >24 - ≤52 >52 ≤12 >12 - ≤24 >24 - ≤52 >52 Time of Onset (Weeks) Time of Onset (Weeks)

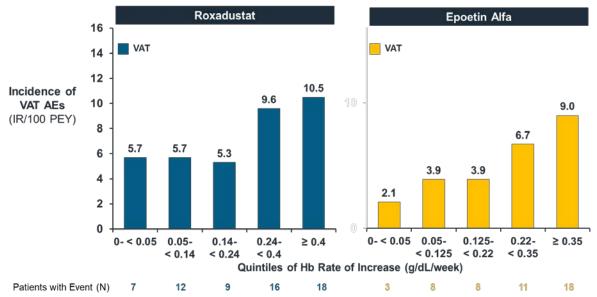
Figure 51: Pooled DD Studies: Adjudicated VAT Adverse Events by Time of Onset

Abbreviations: DD=dialysis-dependent; IR=incidence rate; OT+7=on-treatment plus 7 days; PEY=patient exposure year; VAT=vascular access thrombosis.

Note: Safety Population, OT+7 analysis; DD Pool: Studies 002, 063, 064

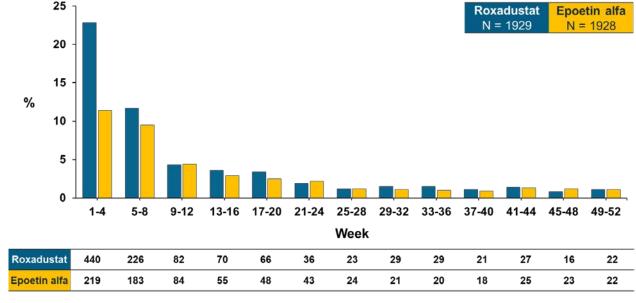
VAT risk was highest with roxadustat treatment early in the studies (Figure 51) when Hb values rose most quickly. During this early study period, roxadustat treatment was associated with a higher Hb rate of rise compared to EPO, which may contribute to the higher observed VAT incidence in roxadustat compared to EPO. Supporting this contention, exploratory analyses indicated that a more rapid rate of Hb rise was associated with a higher risk of VAT events in both roxadustat and EPO groups (Figure 52). Consequently, the higher rate of Hb rise in roxadustat-treated patients may explain the higher VAT risk compared to EPO. Based on this assessment, adjustments to roxadustat starting dose are expected to lower the rate of Hb rise, which will mitigate the risk of VAT.

Figure 52: Pooled DD Studies: Incidence of VAT with Increasing Hb Rate of Increase



Abbreviations: AE=adverse event; DD=dialysis-dependent; Hb=hemoglobin; IR=incidence rate; OT+7=on-treatment plus 7 days; PEY=patient exposure year; VAT=vascular access thrombosis. Note: Safety Population, OT+7 analysis; DD Pool: Studies 002, 063, 064

Figure 53: Pooled DD studies: Proportion of Patients with First Occurrence of Hb Rate of Rise > 2 g/dL within Any 4-Week Period Over Time at Each Visit up to Week 52



Abbreviation: DD=dialysis-dependent.

Note: Full Analysis Set Population, DD Pool: Studies 002, 063, 064.

With respect to the clinical impact in patients with VAT, no patients were reported to discontinue roxadustat due to a VAT event. In addition, the majority of patients with a VAT event did not have a recurrence of the event (71.0% and 70.6% with roxadustat and EPO, respectively).

The risk of VAT associated with roxadustat can be mitigated by making appropriate modifications to the starting dose in order to decrease the incidence of rapid Hb rates of rise. The Sponsor intends to communicate and mitigate this increased risk of VAT in the product labeling. In addition, the importance of regularly monitoring Hb during treatment will be emphasized, in which Hb levels should be monitored at least every 2 weeks when initiating or adjusting therapy until levels are stable, after which monitoring would occur every 4 weeks.

1.6.3.1.2. Deep Vein Thrombosis and Pulmonary Embolism

Kidney disease is a known risk factor for venous thromboembolic events, in particular DVT and pulmonary embolism (PE), which is a complication of DVT. In one study of patients with DD CKD, the rate of DVT was 3.3/100 PY, while the rate of PE was 0.65/100 PY (Molnar et al 2018).

The overall incidence of DVT was low in the roxadustat pivotal studies; however, there was a higher number of DVT events in the roxadustat groups than the comparator groups across the NDD and DD populations. The rates of PE events in the roxadustat groups and comparator groups were low and comparable across the NDD and DD populations (Table 11).

Table 11: NDD and DD Studies: DVT and PE Adverse Events (OT+28)

Preferred Term	Roxac N=2		Placebo N=1884		
NDD Population	n (%) IR/100 PY		n (%)	IR/100 PY	
Deep vein thrombosis or Pulmonary embolism	35 (1.5)	0.9	9 (0.5)	0.4	
Deep vein thrombosis	28 (1.2)	28 (1.2) 0.7		0.2	
Pulmonary embolism	10 (0.4)	0.2	3 (0.2)	0.1	
	Roxadustat N=1940		Epoeti N=1	in Alfa 1940	
DD Population	n (%)		n (%)		
Deep vein thrombosis or Pulmonary embolism	41 (2.1)		36 (1.9)		
Deep vein thrombosis	30 (1.5)		19 (1.0)	
Pulmonary embolism	13 (0.7) 17 (0.9)		0.9)		

Abbreviations: DD=dialysis-dependent; DVT=deep vein thrombosis; IR=incidence rate; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PE=pulmonary embolism; PY=patient years.

Note: Safety Population, OT+28 analysis, NDD Pool: Studies 001, 060,608; DD Pool: Studies 002, 063, 064

Across treatment groups, demographics and baseline characteristics in patients with a DVT and/or PE were generally consistent with what is observed in patients at risk of venous thrombosis.

When assessing the clinical circumstances of these DVT occurrences, it is noted that many of the DVT events occurred around the time of hospitalization, a known at-risk setting for thrombotic events. For example, in the DD pool, 16 of 30 (53.3%) roxadustat-treated patients and 11 of 19 (57.9%) EPO-treated patients with a DVT had the event between 1 day after the patient was hospitalized and 30 days after hospital discharge.

With respect to the clinical impact in patients with DVT and PE, few events led to study treatment discontinuation (Table 12). The majority of patients recovered or were recovering without recurrence of the event, with most patients having received antithrombotic treatment for the event.

Table 12: NDD and DD Studies: Clinical Impact in Patients with DVT/PE

	NDD (C	NDD (OT+28)		T+28)	
	Roxadustat N=2386	Placebo N=1884	Roxadustat N=1940	Epoetin Alfa N=1940	
Category Preferred Term	n (%)	n (%)	n (%)	n (%)	
AEs with fatal outcome					
Deep vein thrombosis	1 (< 0.1%)	0	0	0	
Pulmonary embolism	1 (< 0.1%)	1 (< 0.1%)	4 (0.2%)	5 (0.3%)	
AEs leading to study drug discontinuation					
Deep vein thrombosis	1 (< 0.1%)	0	1 (< 0.1%)	0	
Pulmonary embolism	1 (< 0.1%)	0	2 (0.1%)	3 (0.2%)	
Patients with ≥ 2 recurrent events or who did not recover from first event [non-fatal events only]					
Deep vein thrombosis	1 (< 0.1%)	0	6 (0.3%)	3 (0.2%)	
Pulmonary embolism	2 (< 0.1%)	0	4 (0.2%)	2 (0.1%)	

Abbreviations: AE=adverse event; DD=dialysis-dependent; DVT=deep vein thrombosis; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PE=pulmonary embolism.

Note: Safety Population, OT+28 analysis, NDD Pool: Studies 001, 060,608; DD Pool: Studies 002, 063, 064

Similar to VAT, the Sponsor intends to communicate and mitigate this increased risk of DVT in the product labeling with clinical measures that include adjustments to the roxadustat dosing algorithm in order to decrease the incidence of rapid rates of Hb rise or excursions above target levels. In addition, the importance of regularly monitoring Hb during treatment will be emphasized, in which Hb levels should be monitored at least every 2 weeks when initiating or adjusting therapy until levels are stable, and then every 4 weeks. The clinician is also advised to consider withholding treatment for severe or life-threatening thrombosis and manage all thromboses promptly. In addition, the risk of DVT will be communicated in the Medication Guide to inform patients of the signs and symptoms associated with DVT and when to seek medical help.

1.6.3.2. Seizures

Seizures are more common among patients with CKD than the general population (Lakshman et al 2016). A standardized Medical Dictionary for Regulatory Activities query was conducted for convulsions to capture all preferred terms related to seizures. The incidence of seizures was higher in the roxadustat groups than the comparator groups across the NDD and DD populations (Table 13). The majority of the roxadustat-treated patients recovered with continued treatment and without seizure recurrence. The occurrence of seizures in roxadustat-treated patients was higher in a subset of patients with a baseline medical history of seizures. The Sponsor intends to mitigate this risk by providing 'Warnings and Precautions' about seizures in the product labeling as detailed in Section 1.6.

Table 13: NDD and DD Studies: Seizure Adverse Events

		ndustat 2386		acebo =1884
NDD Population	n (%)	IR/100 PY	n (%)	IR/100 PY
Convulsions AEs (SMQ) (OT+28)	26 (1.1)	0.6	4 (0.2)	0.2
Convulsions SAEs (SMQ) (OT+28)	10 (0.4)	0.2	1 (0.1)	0.0
Convulsions in patients with a reported history of seizure	3/31 (9.7)	6.2	0	0
	Roxadustat N=1940		Epoetin Alfa N=1940	
DD Population	n (%)		n	(%)
Convulsions AEs (SMQ) (OT+28)	45 (2.3)		34 (1.8)	
Convulsions SAEs (SMQ) (OT+28)	26 (1.3)		20 (1.0)	
Convulsions in patients with a reported history of seizure	9/38	(23.7)	5/46	5 (10.9)

Abbreviations: AE=adverse event; IR=incidence rate; DD=dialysis-dependent; MedDRA=Medical Dictionary for Regulatory Activities; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PY=patient years; SMQ=standardized MedDRA query.

Note: Safety Population, OT+28 analysis; NDD Pool: Studies 001, 060,608; DD Pool: Studies 002, 063, 064.

1.6.3.3. Serious and Fatal Infections

Infections are a common and important source of morbidity and mortality in patients with CKD. Risk for infections increases as CKD becomes more severe and is higher in dialysis compared to non-dialysis patients. In the roxadustat Phase 3 clinical program, AEs and serious AEs (SAEs) in the System Organ Class of Infections and Infestations were common in both treatment groups in the NDD and DD pools.

In the pooled NDD studies, the incidence rate of serious infections was 12.4 vs 10.6/100 PY for roxadustat and placebo in OT+28, respectively (Table 14). Adjudicated fatal infections were reported at a higher frequency in patients treated with roxadustat (1.4/100 PY in OT+28) than placebo (0.7/100 PY in OT+28). The majority (23/39) of fatal infections in the placebo group occurred following the on-treatment analysis period, which is not unexpected as the subpopulations of patients at a higher risk for infection were most affected by differential discontinuation of study drug. Importantly, the incidence of fatal infections was similar between roxadustat- and placebo-treated patients in the US (0.3/100 PY vs 0.5/100 PY, respectively); the imbalance between groups comes from the ex-US patient population (1.7/100 PY vs 0.7/100 PY, respectively).

In the pooled DD studies, adjudicated fatal infections were reported at a similar frequency in patients treated with roxadustat (2.4% in OT+28) compared to EPO (2.4% in OT+28) and serious infections were reported in 24.4% vs 24.6% of patients in OT+28, respectively. In contrast to the NDD studies, there was no difference in the incidence of fatal infection by treatment group.

Table 14: NDD and DD Studies: Infection Adverse Events

		Roxadustat N=2386		cebo 1884
NDD Population (On-Study)	n (%)	IR/100 PY	n (%)	IR/100 PY
Infection/Infestation AE (SOC)	1318 (55.2%)	50.8	942 (50.0%)	47.2
Infection/Infestation SAE (SOC)	509 (21.3%)	13.1	343 (18.2%)	12.1
Infection Death (adjudication)	87 (3.6%)	2.0	39 (2.1%)	1.2
NDD Population (OT + 28)	n (%)	IR/100 PY	n (%)	IR/100 PY
Infection / Infestation AE (SOC)	1255 (52.6%)	51.3	798 (42.4%)	47.4
Infection / Infestation SAE (SOC)	452 (18.9%)	12.4	243 (12.9%)	10.6
Infection Death (adjudication)	55 (2.3%)	1.4	16 (0.8%)	0.7
		Roxadustat N=1940		in Alfa 1940
DD Population (OT+28)	n (n (%)		%)
Infection/Infestation AE (SOC)	972 (972 (50.1)		(50.2)
Infection/Infestation SAE(SOC)	473 (473 (24.4)		(24.6)
Infection Death (adjudication)	47 ((2.4)	46 ((2.4)

Abbreviation: AE=adverse event; DD=dialysis-dependent; IR=incidence rate; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PY=patient years; SAE=serious adverse event; SOC=System Organ Class. Note: Safety Population, OT+28 analysis; NDD Pool: Studies 001, 060,608; DD Pool: Studies 002, 063, 064.

The risk of serious infections, including fatal infections, in the NDD population increases with lower baseline eGFR. As shown in Table 15, patients in the roxadustat group with baseline eGFR < 10 mL/min/1.73 m² and those who had started dialysis had a higher incidence of fatal infections. Roxadustat patients with the lowest baseline eGFR and those who required dialysis initiation were substantially more likely to remain on study drug compared to placebo patients, which had the potential to introduce bias and may have contributed to the observed higher incidence rate of fatal infection in roxadustat patients in the NDD population. The incidence of fatal infection was similar for roxadustat and EPO in the DD population, and rates of serious infection were generally similar for roxadustat and comparator across the population.

Table 15: Pooled NDD Studies: Fatal Infection Adverse Events by Baseline eGFR

	OT+28				On-S	Study			
	Roxadu N=23					Roxadustat N=2386		Placebo N=1884	
	n/N (%)	IR	n/N (%)	IR	n/N (%)	IR	n/N (%)	IR	
Infection Death									
Baseline eGFR: < 10	21/481 (4.4%)	3.0	2/358 (0.6%)	0.6	27/481 (5.6%)	3.1	5/358 (1.4%)	0.7	
Baseline eGFR: ≥ 10	34/1905 (1.8%)	1.0	14/1526 (0.9%)	0.7	60/1905 (3.1%)	1.5	34/1526 (2.2%)	1.1	
Infection Death									
After dialysis initiation (NDD-ID)	18/747 (2.4%)	2.4	2/351 (0.6%)	0.9	34/870 (3.9%)	3.1	11/611 (1.8%)	1.4	
Did not initiate or prior to dialysis (NDD-NDD)	35/2386 (1.5%)	1.1	14/1884 (0.7%)	0.6	53/2386 (2.2%)	1.4	28/1884 (1.5%)	1.0	

Abbreviations: eGFR=estimated glomerular filtration rate; ID=incident dialysis; IR=incidence rate; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days.

Note: Safety Population, OT+28 analysis or On-study analysis (Studies 001, 060, 608, N=4270)

In the NDD Study 610, the incidence of infection SAEs was higher for roxadustat compared to darbepoetin alfa; however, the incidence rate of fatal infections was similar compared to darbepoetin alfa (see Section 7.2).

Overall, the fatal infection results from the pooled NDD studies are inconsistent with the fatal infection results for the pooled DD studies and Study 610 where incidence of fatal infection was similar for roxadustat and comparator, suggesting that bias due to differential treatment discontinuation may have confounded the fatal infection comparisons in the pooled placebo-controlled NDD studies.

The Sponsor intends to provide 'Warnings and Precautions' related to the potential risk of infection in the product labeling. More specifically, labeling language to suggest avoidance of initiating treatment with roxadustat in patients with an active severe or serious infection, advice to patients to promptly report to their healthcare provider if they have signs or symptoms of an infection, and if an infection is suspected, advice to the healthcare practitioner to evaluate the patient and treat promptly.

1.7. Risk Management

In the post-approval setting, the Sponsor has a comprehensive plan in place to enable rapid evaluation of the safety profile of roxadustat in order to characterize and communicate pertinent safety data appropriately to healthcare providers and patients. Safety outcomes that will be specifically monitored during the post-approval period include thrombotic events (eg, VAT and DVT), seizures, and serious infections. These risk management activities are described in further detail below, including recommendations for changes to roxadustat starting dose and planning for post-marketing studies.

1.7.1. Risk Minimization

The Sponsor plans to communicate all relevant safety information and recommendations for risk mitigation associated with the use of roxadustat in the product labeling (Prescribing Information) and

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Medication Guide for healthcare providers and patients, respectively. The Sponsor also plans to communicate risks in educational materials for healthcare providers.

Important safety information includes:

- Thrombotic events (eg VAT and DVT): This risk can be mitigated by reducing starting doses in order to decrease the incidence of rapid Hb rates of rise (See Section 1.7.3). Monitor Hb during treatment (ie, when initiating or adjusting therapy, monitor Hb levels at least every 2 weeks until stable, then monitor every 4 weeks). Consider withholding for severe or life-threatening thrombosis and manage all thromboses promptly. Advise patients to contact their healthcare provider for signs and symptoms of thrombosis.
- Seizures: Advise patients to promptly report new onset seizures, premonitory symptoms, or
 increase in seizure frequency or severity to their healthcare provider. Patients with a history of
 seizure should be treated with caution.
- Serious Infections: Avoid starting roxadustat in patients with an active severe or serious infection. Monitor patients for signs and symptoms of infection and promptly treat. Advise patients to contact their healthcare provider for signs and symptoms of an infection.

1.7.2. Post-marketing Surveillance

Safety risks will continue to be monitored and evaluated in the post-approval setting, and will include the following:

- Adverse event reporting: All individual case safety reports from spontaneous sources will
 captured in a validated safety database and relevant cases (eg, SAEs) will be reported to FDA's
 Adverse Event Reporting System. For spontaneous reports, targeted follow-up questionnaires
 will be used to collect additional specific information for events of interest (ie, DVT, VAT,
 seizures, serious infections).
- Safety signal management: Safety surveillance and signal detection activities, which includes a
 monthly screening and evaluation of the Sponsor's global safety database assessing serious and
 non-serious AEs reported from all sources (eg, clinical trials, spontaneous) will be performed.
 In addition, monthly safety assessments evaluate the global medical and scientific literature
 with regards to non-clinical and clinical reports. Review of global health authority safety
 databases (eg, FDA's Adverse Event Reporting System and Vigibase) are also conducted when
 potential signals are evaluated. Any confirmed signals will be communicated with the FDA.
- Aggregate Reports: Cumulative reviews of events of interest will be summarized in periodic reports (eg, Periodic Benefit-Risk Evaluation Report) and will be submitted to the FDA.

In addition to the activities listed above, the Sponsor is evaluating potential activities to characterize thrombosis risk with roxadustat treatment in the real-world setting at the newly recommended dosing regimen.

The Sponsor will continuously evaluate, communicate, and mitigate known risks associated with the use of roxadustat. The Sponsor is also committed to working with the FDA on the development and implementation of appropriate activities/measures.

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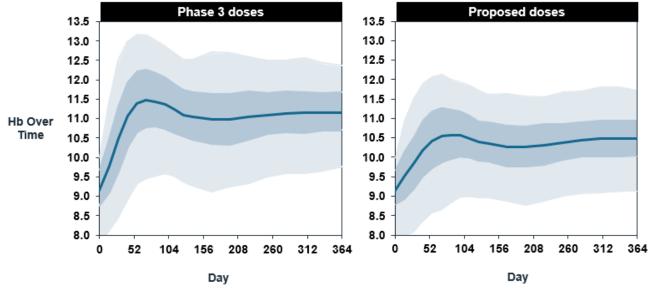
1.7.3. Starting Dose Reduction and Lowering Hb Target

Dosing recommendations for ESAs were modified in the post-marketing setting following evidence of an increased CV risk associated with higher Hb targets. Revised Hb targets were subsequently lowered, and Hb values > 11 g/dL are no longer a target for ESAs, though this has not been rigorously tested in randomized-controlled trials. In the roxadustat program, in both the NDD and DD studies, roxadustat-treated patients were treated to Hb targets of 10.5–12 g/dL. Similar to the strategy employed for ESAs, the Sponsor proposes to lower Hb targets in roxadustat-treated patients to 10–11 g/dL, which will lead to a lower effective dose and maintain the reduction in the risk of transfusion risk. In addition, like for ESAs, the Sponsor is recommending that the number of sequential dose increases in non-responsive patients is limited, to 3.

As noted in Section 1.6.3.1, rapid rise of Hb was more common in the first 12 weeks of treatment than in the later phases of the studies and was associated with a greater risk of thrombotic events. The Hb response in this early phase was mainly affected by the starting dose. As very few actual starting doses (non-randomized) were utilized in the Phase 3 program, the Sponsor conducted modeling and simulation to estimate the effect of a range of potential starting doses on Hb performance and rapid rise. A semi-mechanistic-pharmacodynamic longitudinal mixed-effect model previously used in Phase 3 planning was re-evaluated and re-estimated using the new Phase 3 data. The model describes the time-course of Hb changes after the administration of roxadustat and is represented schematically in Figure 72 in Section 11.

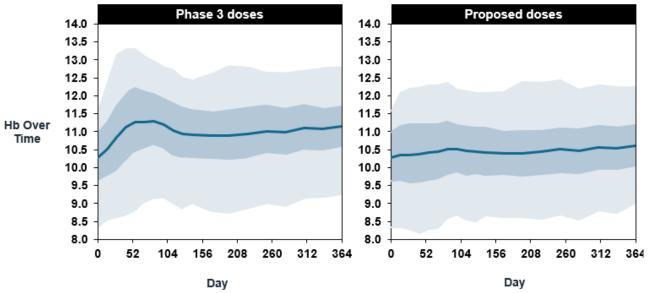
Figure 54 displays simulated Hb over time for ESA-untreated patients starting roxadustat, and Figure 55 for patients switching to roxadustat from ESA treatment. The graphs compare Hb dynamics with the doses utilized in the Phase 3 program and with the lower recommended starting doses. The reduced starting doses decrease the initial peak in Hb and rate of rise in both populations without diminishing longer-term efficacy.

Figure 54: Simulated Mean Hb Values with Roxadustat in Previously ESA-untreated Patients



Abbreviations: ESA=erythropoiesis-stimulating agent; Hb=hemoglobin. Note: Solid line is mean. Grey areas depict 5, 25, 75, 95% quantiles.

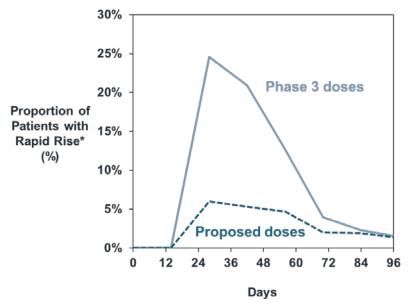
Figure 55: Simulated Mean Hb Values in Patients Converting from ESA to Roxadustat



Abbreviations: ESA=erythropoiesis-stimulating agent; Hb=hemoglobin. Note: Solid line is mean. Grey areas depict 5, 25, 75, 95% quantiles.

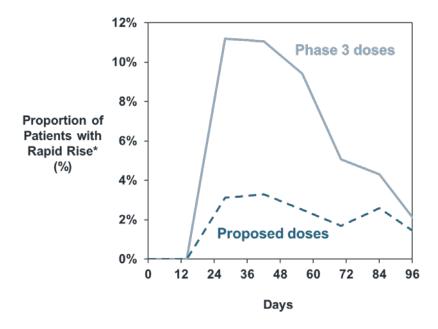
Figure 56 and Figure 57 display the incidence of rate of rise > 2 g/dL over 4 weeks for the ESA-untreated patients and ESA converters, respectively. The Phase 3 doses and the recommended lower starting doses are shown. The modeling and simulation data show reduction in the initial incidence of rapid rate of rise of Hb by at least two-thirds in both ESA-untreated and ESA conversion patients.

Figure 56: Proportion of Roxadustat Patients (Previously Untreated with ESA) with Rapid Rate of Hb Rise, Phase 3 Dose Compared to Proposed Dose



Abbreviations: ESA=erythropoiesis-stimulating agent; Hb=hemoglobin.

Figure 57: Proportion of Patients Converting from ESA to Roxadustat with Rapid Rate of Hb Rise, Phase 3 Doses Compared to Proposed Doses



Abbreviations: ESA=erythropoiesis-stimulating agent; Hb=hemoglobin.

The Sponsor plans reduced starting doses to mitigate the risk of VAT and other thrombotic complications and is evaluating potential post-marketing activities to assess Hb rate of rise and

^{*}Rapid rise: 4-week increase > 2 g/dL.

^{*}Rapid rise: 4-week increase > 2 g/dL.

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thrombosis risk with these changes. Additionally, the Sponsor recommends to lower Hb target in roxadustat-treated patients to 10–11 g/dL and to limit the number of successive dose increases in patients who are not responding to roxadustat. These changes are anticipated to reduce doses of roxadustat and improve the roxadustat safety profile, while retaining efficacy and the desired reduction in transfusion risk.

1.8. Benefit-Risk Summary

Roxadustat is a first-in-class, oral therapy that provides treatment of CKD anemia with the benefit of a novel mechanism of action that consistently corrects and maintains Hb across the spectrum of NDD and DD CKD anemia with an acceptable safety profile. In contrast to parenteral ESAs, which exogenously replace erythropoietin, roxadustat is a small molecule, reversible inhibitor of HIF-PH that stimulates HIF mediated erythropoiesis in a way that mimics the body's natural response to low oxygen environments by inducing endogenous erythropoietin and increasing iron availability.

The current paradigm and standard of care for anemia treatment in NDD CKD has limitations. By requiring frequent travel to a healthcare facility for many individuals, the standard of care over the last 30 years produces many barriers to effective anemia treatment. Standard treatment for NDD CKD anemia generally requires treatment in a healthcare setting every week to every 3 weeks, which is inconvenient and may preclude treatment for many patients. Due in part to these limitations, many patients are untreated, and rates of transfusions – which require substantial healthcare utilization, have significant risks, and can decrease access to kidney transplantation – are unacceptably high. Roxadustat offers patients with NDD CKD an oral, convenient, home therapy that provides a coordinated erythropoiesis involving both erythropoietin production and increased iron utilization, to benefit patients whose disease is sub-optimally managed in the current real-world setting.

Roxadustat provides benefit as it mitigates the IV iron requirement and lowers the risk of RBC transfusions. In the roxadustat clinical development program, all pivotal studies met the primary efficacy endpoint. The NDD trials demonstrated statistically significant treatment differences favoring roxadustat compared to placebo, providing patients with consistent increases in Hb regardless of baseline iron repletion status or inflammation. Importantly, patients treated with roxadustat achieved clinically meaningful reductions in transfusions. In the DD clinical trials, roxadustat was comparable in efficacy and safety to EPO.

Unlike ESAs, roxadustat achieved efficacy in patients with elevated hsCRP and those with normal hsCRP without a need for dose increase. In addition, roxadustat is an effective treatment for patients with markers of hyporesponsiveness to ESAs including increased ferritin and hepcidin. Outside of clinical trials, these patients are currently devoid of clinical options beyond higher doses of ESAs and additional IV iron or marked transfusion requirement. These individuals will benefit from a treatment with a different mechanism of action to raise their Hb levels.

Roxadustat demonstrated comparable CV safety to placebo in patients with NDD CKD and to EPO in patients with DD CKD. Patients treated with roxadustat had increased rates of VAT and DVT compared to EPO. Increased thrombosis risk was observed with higher rates of Hb rise in both roxadustat and EPO-treated patients, supporting the notion that reductions in the incidence of rapid rates of Hb rise can lower thrombosis risk in roxadustat-treated patients. More roxadustat-treated patients had seizures versus comparators, and patients with a history of seizure should be treated with roxadustat with caution. Increased fatal infection was noted for roxadustat compared with placebo in the NDD population; fatal infection risk, however, was not observed compared to darbepoetin. In

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addition, this this finding was not duplicated in the DD population, where rates were generally similar between roxadustat and comparator. In order to improve roxadustat's safety profile while maintaining efficacy and reducing transfusion risk, the Sponsor proposes plans to use lower starting doses, to treat to lower Hb targets, and to limit the number of consecutive dose increases in patients not responding to roxadustat. The Sponsor will continuously evaluate, communicate, and mitigate known and potential risks associated with the use of roxadustat.

Overall, the roxadustat clinical program provided efficacy and safety data to support its use to increase and maintain Hb levels for patients across the continuum of CKD anemia. Roxadustat offers a novel mechanism of action for the treatment of CKD anemia with unique benefits compared to ESAs and the convenience of an oral treatment that can be used to support home hemodialysis, peritoneal dialysis, and non-dialysis patients. Based on the totality of the evidence, the benefit-risk is positive for roxadustat in patients with NDD and DD CKD who need correction of their anemia.

SUPPLEMENTAL INFORMATION

2. PRODUCT DESCRIPTION

2.1. Dosage

The roxadustat formulation is proposed in 5 dose strengths of 20, 40, 50, 70, and 100 mg tablets for oral administration. For ESA-naïve patients or those not currently receiving stable doses of ESA, the recommended starting dose of roxadustat is based on body weight. For patients converting from an ESA, the recommended starting dose of roxadustat is based on their prior ESA dose.

The dose range is 20 mg to 400 mg per administration.

Maximum Recommended Dose

- Patients not on dialysis: Not exceed a dose of 3 mg/kg or 300 mg TIW, whichever is lower
- Patients on dialysis: Not exceed a dose of 3 mg/kg or 400 mg TIW, whichever is lower

2.2. Product Overview

2.2.1. Pharmaceutical and Biological Properties of Roxadustat

Roxadustat is a new chemical entity and the first in a new pharmacologic class of small molecule therapeutics (Kang et al 2015). As shown in Figure 58, roxadustat is an N-acyl glycine resulting from the formal condensation of the amino group of glycine with the carboxy group of 4-hydroxy-1-methyl-7-phenoxyisoquinoline-3-carboxylic acid. The chemical classification/formula and other key characteristics of roxadustat are provided in Table 16.

Figure 58: Structural Formula of Roxadustat

Table 16: Key Characteristics of Roxadustat

International Non-proprietary Name/ Alternative Names	roxadustat (FG-4592)
Chemical Name	[(4-hydroxy-1-methyl-7-phenoxyisoquinoline-3-carbonyl) amino] acetic acid
Chemical formula	$C_{19}H_{16}N_2O_5$
Chemical Abstract Service Registry Number	808118-40-3
Molecular weight	352.34 g/mol
Class	Amide; antianemia; carboxylic acid; isoquinoline; small molecule
Mechanism of action	Binds to and potently inhibits HIF-PHD, reducing HIF breakdown and promoting its activity
Pharmacokinetics	Exposure increases dose-dependently (approximately proportional to dose) across 1–4 mg/kg dose range; half-life was 8–12 h
Pharmacodynamics	Dose-dependently increase Hb levels, reduce hepcidin and cholesterol levels and transiently increase endogenous EPO levels within or near physiologic range

2.3. Mechanism of Action

Roxadustat is a novel, orally bioavailable, potent and reversible HIF-PH inhibitor (HIF-PHI) that transiently induces HIF stabilization and leads to a functional HIF transcriptional response that mimics the erythropoietic response associated with exposure of humans to intermittent hypoxia. HIF induces expression of not only erythropoietin, but also the erythropoietin receptor and proteins that promote iron absorption and recycling from the macrophage iron storage system (Peyssonnaux et al 2008). Thus, roxadustat pharmacologically stimulates erythropoiesis via the HIF pathway and in a manner consistent with the physiologic response to hypoxia, but under normoxic conditions.

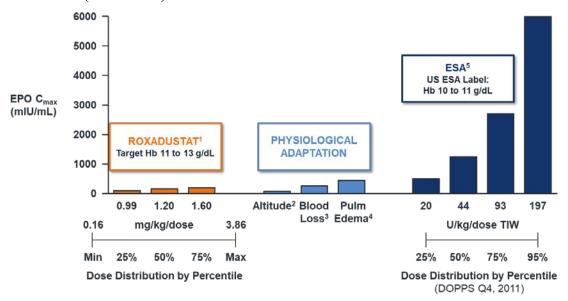
Roxadustat also has the potential to effectively treat anemia caused by inflammation-induced functional iron deficiency, which is typically hyporesponsive to ESAs. In these conditions, iron availability for erythropoiesis is reduced due to a number of inflammatory mediators. Because HIF-PHIs such as roxadustat alter expression not only of the erythropoietin gene, but also of genes regulating iron metabolism, it is postulated that roxadustat may be effective in treating these anemias as well (Siddiq et al 2005).

Chronic hypoxia and intermittent hypoxia induce different sets of genes associated with HIF transcriptional activity, presumably because intermittent stimulation allows the restoration of HIF degradation, turnover, and inactivation. Transient activation of HIF thereby precludes sustained gene expression and the induction of genes that are expressed late after HIF activation, as well as expression of additional genes that are secondary to activation of HIF-dependent genes. Both nonclinical and clinical studies of roxadustat have successfully used the intermittent dosing paradigm to induce selective erythropoiesis and to optimize the Hb dose response. Furthermore, roxadustat was selected for development over other HIF-PHI candidate molecules based on an optimal biodistribution profile that enhances its selective action (eg, kidney [erythropoietin production], bone marrow [increase in erythropoietin receptors], duodenum [iron transport], and liver [erythropoietin and transferrin production and down-regulation of hepcidin]).

The physiologic mechanisms underlying the effects of roxadustat on erythropoiesis are distinct from those of ESAs, and these differences result in several potential advantages over ESAs beyond the convenience of oral therapy.

- Increase in the number of erythropoietin receptors in the bone marrow
- Improved iron metabolism and bioavailability
- Effective erythropoiesis at levels comparable to physiologic plasma erythropoietin concentrations (~10 to 20-fold lower than the supra-physiologic levels associated with parenteral ESA therapy) (Figure 59)
- Effective erythropoiesis in the presence of inflammation
- Reduction in total and low-density lipoprotein (LDL) cholesterol

Figure 59: Circulating Erythropoietin Exposure with Roxadustat-Treated Patients with CKD and ESRD versus Reported ESA Dosing Patterns in ESRD (2005–2009)



Abbreviations: CKD=chronic kidney disease; C_{max} =maximal serum concentration; EPO=epoetin alfa; ESA=erythropoiesis-stimulating agent; ESRD=end-stage renal disease; Hb=hemoglobin; Max=maximum; Min=minimum; TIW=3 times per week.

¹C_{max} data for roxadustat estimated for a subset of 243 patients who achieved Hb response and were dosed at expected therapeutic doses; ²Milledge and Cotes 1985; ³Goldberg et al 1993, Maeda et al 1992; ⁴Kato et al 1994; ⁵Based on Flaharty et al. (1990).

3. REGULATORY AND DEVELOPMENT HISTORY

3.1. Regulatory Milestones

Key regulatory milestones between FDA and FibroGen in the clinical development of roxadustat are summarized in Table 17.

Table 17: Key Regulatory Milestones in Roxadustat Clinical Development

Dates	Discussion
04/17/2006	IND submitted under section 505 (b)(i) of the Food, Drug, and Cosmetic Act for roxadustat.
07/17/2012	End-of-Phase (EOP) 2 meeting: FDA requested that the roxadustat clinical development program be powered to assess CV safety for the NDD and DD CKD populations separately as a result of CV safety concerns for ESAs. To comply with this request, the sample size was increased in planned studies, new studies were added to the program, and study durations were extended. Independent CV endpoint adjudication was instituted, and FDA advised that while it would use MACE as its primary safety endpoint for analysis, the Sponsor could choose a different primary safety endpoint.
11/20/2012	FDA agreed that while placebo-controlled Phase 3 studies must be double-blind, open-label studies were acceptable for ESA comparator studies due to practical and ethical issues with a double-dummy design. FDA advised that open-label studies could contribute to the CV safety analysis since MACE is an objective endpoint that is not subject to ascertainment bias.
05/09/2014	FDA reiterated its preference for MACE as the primary safety endpoint. The choice of non-inferiority margin for the CV safety analysis was discussed, but no acceptable non-inferiority margin was agreed upon.
05/12/2014	Dosing regimens of once weekly, twice weekly, and TIW were initially investigated in the NDD Phase 3 program. At the May 2014 meeting, FDA recommended a single maintenance dosing regimen of TIW. Patients were converted to TIW dosing in Study 060 while patients were maintained on their original regimen in Study 608.
06/26/2017	FDA expressed concern that Study 1517-CL-0613 could be difficult to evaluate in pooled CV safety analysis as noted above and thus is not included in the DD pool.
07/30/2019	Pre-NDA meeting: The purpose of this meeting was to discuss the New Drug Application for roxadustat tablets for the treatment of anemia due to CKD. FDA advisement:
	The final Pooled Safety Analysis Plan safety pooling strategy in the NDD CKD population appears reasonable.
	The ITT analysis set for the MACE and MACE+ endpoints is preferred for analyses of the NDD CKD population.
	The final pooling strategy for analysis of CV safety (which removed Study 1517-CL-0613) in the DD CKD population appears reasonable.
	The OT+7 analysis set appears to be acceptable for analysis of the MACE and MACE+ endpoints in the DD CKD population, although sensitivity analyses should be done using the OT+28 analysis set.
12/20/2019	NDA submitted.

Abbreviations: CV=cardiovascular; DD=dialysis-dependent; ESA=erythropoiesis-stimulating agent; FDA=Food and Drug Administration; IND=investigational new drug; ITT=intent-to-treat analysis set; MACE=major adverse cardiac event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure NDA=New Drug Application; NDD=non-dialysis-dependent; OT+7=on-treatment plus 7 days; OT+28=on-treatment plus 28 days; TIW=3 times per week.

4. CLINICAL PHARMACOLOGY

4.1. Clinical Pharmacology Studies

The global clinical pharmacology program to characterize roxadustat pharmacokinetic (PK) and pharmacodynamic parameters related to erythropoiesis and absorption, distribution, metabolism, and elimination/excretion includes:

- 1. Nonclinical pharmacology studies including 19 in vitro and ex vivo studies using human biomaterials.
- 2. Clinical pharmacology studies including 26 studies in healthy subjects, 1 study in patients with hepatic impairment, 3 studies in patients with severe renal impairment or ESRD, as well as clinical Phase 2/3 studies in patients with NDD CKD or DD CKD.

A comprehensive summary of key clinical pharmacology findings is provided below.

4.2. Pharmacokinetics

4.2.1. General Pharmacokinetic Properties

The PK and metabolic profile of roxadustat was evaluated in healthy subjects and patients with severely impaired renal function (eGFR $< 30 \text{ mL/min/1.73 m}^2$), including patients with ESRD requiring hemodialysis or hemodiafiltration. Roxadustat plasma exposure (area under the curve [AUC] and maximum plasma concentration [C_{max}]) is dose-proportional from 20 to 280 mg (0.3 to 4.0 mg/kg, body weight); reaching a steady-state within one week with minimal accumulation. Roxadustat AUC is approximately 2-fold higher in patients with NDD or DD CKD than in healthy subjects, but C_{max} is comparable.

4.2.2. Absorption, Distribution, Metabolism, and Elimination

Absorption: Roxadustat is rapidly absorbed and bioavailable with C_{max} achieved at 2 h post-dose (fasted) in healthy subjects. Intake with food reduces the C_{max} by 25% but does not affect roxadustat bioavailability. In vivo studies in healthy human subjects have demonstrated that \geq 92% of the drug-related material in plasma is parent drug at 0.5 to 1 h post-dose from a single oral dose, suggesting that roxadustat is absorbed largely intact. In addition, recovery of Phase-1 oxidative and Phase-2 conjugated metabolites from urine and feces, accounting for 60% of the dose from a single oral dose is indicative of a high degree of absorption of roxadustat from the gastrointestinal tract.

<u>Distribution</u>: Roxadustat is highly bound (~99%) to human plasma proteins, predominantly to albumin. In patients with severe renal impairment and ESRD on hemodialysis or hemodiafiltration, the mean unbound % of roxadustat in plasma is slightly increased compared with healthy subjects (1.1 % vs 0.9%) Dialysis does not appear to influence the in vivo protein binding of roxadustat but higher levels of unbound roxadustat have been seen in patients with moderate hepatic impairment. The distribution of roxadustat into RBCs is low, with a blood-to-plasma ratio of 0.5 after single-dose administration of radiolabeled roxadustat.

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Metabolism: Roxadustat is metabolized by cytochrome P450 (CYP)2C8 and uridine diphosphate-glucuronosyltransferase (UGT)1A9. Roxadustat is primarily metabolized through 2 main metabolic pathways: hydroxylation/oxidation followed by sulfation, producing metabolites 4'-hydroxy roxadustat and 4'-O-sulfate conjugates of 4'-hydroxy roxadustat, together accounting for 20% of the radioactive dose. The O-glucuronidation produces metabolite 4-O- β -glucuronide of roxadustat, representing 28% of the dose. Minor metabolic routes included glucosidation producing 4-O- β -glucoside of roxadustat (8.1% of the dose), acyl glucuronidation producing acyl-1-O- β -glucuronide of roxadustat (0.6% of the dose), and demethylation producing N-descarboxymethyl roxadustat oxide and N-descarboxymethyl roxadustat (together ~3.6% of the dose).

<u>Elimination/Excretion</u>: The elimination and excretion of roxadustat and its metabolites involves multiple pathways including metabolism, biliary and/or intestinal clearance, and renal clearance (CLR). Roxadustat has an apparent total body clearance of 1.1 and 1.4 L/h in patients with NDD CKD and DD CKD respectively, compared with 2.3–2.6 L/h in healthy subjects. In feces, intact roxadustat was the major component (28%) of the dose, representing unabsorbed drug, biliary excretion of intact drug, and/or deconjugated (glucuronide) metabolites. The effective half-life of roxadustat is approximately 10 hours in healthy subjects, and 15 hours in patients with CKD.

4.2.3. Intrinsic Factors

Based on a population PK analysis of 2,855 subjects from 4 Phase 3 studies, no clinically relevant differences in the PK of roxadustat were observed based on age, sex, race, body weight, renal function (eGFR), or dialysis status in patients with anemia due to CKD.

<u>Hepatic impairment</u>: Following single-dose administration of 100 mg roxadustat in patients with moderate hepatic impairment (Child-Pugh Class B) and subjects with normal renal function, roxadustat AUC was increased by 23% and C_{max} decreased by 16% relative to healthy subjects matched for age, sex, and BMI. Roxadustat unbound fraction was increased in patients with moderate hepatic impairment (1.1% vs 0.8%), resulting in an increase in mean unbound C_{max} and AUC_{inf} of 16% and 70%, respectively, compared with matched healthy subjects. Roxadustat PK has not been studied in patients with severe hepatic impairment (Child-Pugh Class C). A lower starting dose is recommended when prescribing roxadustat to patients with moderate hepatic impairment.

Renal Impairment: A positive correlation was observed between roxadustat PK parameters (CL/F, CLR, and unbound CL/F and CLR) and renal function (eGFR). Most patients (\sim 70%) included in the analysis had an eGFR of \leq 15 mL/min/1.73 m².

4.2.4. Extrinsic Factors

4.2.4.1. In Vitro Findings

Roxadustat is a substrate of CYP2C8 and UGT1A9 enzymes, breast cancer resistance protein (BCRP), organic anion transporting polypeptide (OATP)1B1, and organic anion transporter (OAT)1 and OAT3. Roxadustat inhibits CYP2C8, BCRP, OATP1B1, and OAT3,

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but showed no inhibition of other CYP metabolizing enzymes or transporters at clinically relevant concentrations, in vitro. Roxadustat does not induce CYP enzymes in vitro.

4.2.4.2. Effect of Other Drugs on Roxadustat

Metabolism- and transporter-based drug interactions were studied with gemfibrozil (CYP2C8 and OATP1B1 inhibitor) and probenecid (UGT and OAT inhibitor) in healthy subjects. Results from these studies were used to extrapolate findings to other concomitant medications or products sharing the same drug-drug interactions properties. In addition, population PK analysis of data obtained from Phase 3 clinical studies was used to characterize the impact of observed or anticipated interactions with phosphate binders, oral iron, clopidogrel and perpetrators of CYP2C8, UGT1A9, or OATP1B1 in the target population.

4.2.4.2.1. Phosphate Binders

Coadministration of phosphate binders and roxadustat decreased the absorption of roxadustat (excluding lanthanum carbonate hydrate). However, this effect can be mitigated by administering phosphate binders and roxadustat at least one hour apart.

4.2.4.2.2. Gemfibrozil

Coadministration of roxadustat with gemfibrozil (CYP2C8 and OATP1B1 inhibitor) in healthy subjects increased roxadustat AUC by 2.3-fold and C_{max} by 1.4-fold. The interaction between roxadustat and gemfibrozil or other inhibitors of CYP2C8 or OATP1B1 can be mitigated by regular monitoring of Hb levels in conjunction with dose adjustment according to roxadustat dose adjustment guidelines.

4.2.4.2.3. Probenecid

Coadministration of roxadustat with probenecid (UGT1A9, OAT1, and OAT3 inhibitor) increased roxadustat AUC by 2.3-fold and C_{max} by 1.4-fold and prolonged the half-life by 2.5 h. The interaction between roxadustat and probenecid or other inhibitors of OAT1, OAT3, or UGT1A9 or inducers of UGT1A9 can be mitigated by regular monitoring of Hb levels in conjunction with dose adjustment according to roxadustat dose adjustment guidelines. Probenecid is contraindicated for use in patients with severe renal impairment.

4.2.4.2.4. Other Drugs Without Clinically Meaningful Interactions

Roxadustat exposure was not affected by coadministration with oral iron (from population PK analysis only), clopidogrel (from population PK analysis only), Kremenzin[®], or lanthanum carbonate hydrate. Coadministration of omeprazole with roxadustat did not result in a clinically significant drug-drug interaction.

4.2.4.3. Effect of Roxadustat on Other Drugs

Coadministration of roxadustat with 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (simvastatin, rosuvastatin and atorvastatin) increased plasma exposure of simvastatin, simvastatin acid (active metabolite of simvastatin). Time-separated administration of simvastatin and roxadustat did not reduce the interaction observed with simultaneous administration. These results indicate that roxadustat moderately inhibit BCRP

and OATP1B1. Based on the observed interaction, it is recommended that the maximum daily dose of statins should be reduced.

The PK exposure of bupropion, rosiglitazone, and S-warfarin (probe substrates for CYP2B6, CYP2C8 and CYP2C9, respectively) were not affected by coadministration with roxadustat.

4.3. Pharmacodynamics

4.3.1. Pharmacodynamic Markers of Biologic Activity

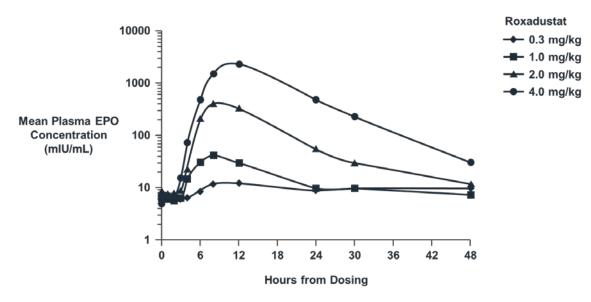
4.3.1.1. Hemoglobin

The purpose of roxadustat treatment was to raise and/or maintain Hb concentrations within the target range of 10 to 12 g/dL. Hb data from Phase 3 studies are the primary efficacy endpoints and are discussed in Section 5.

4.3.1.2. Erythropoietin

Data from the Phase 1 and Phase 2 studies have shown that single and repeated intermittent administration of roxadustat resulted in transient increases in EPO, which returned to baseline at approximately 48 h post-dose. Mean maximum EPO (EPO_{max}) levels increased more than proportionally with dose and were generally achieved approximately 8–12 h post-dose (Figure 60).

Figure 60: Plasma Endogenous EPO Concentration-Time Curve Profile in Healthy Subjects



Abbreviation: EPO=erythropoietin.

4.3.1.3. Hepcidin

Hepcidin, an iron metabolism regulating protein, is increased during inflammation and contributes to a lack of iron availability and therefore inadequate erythropoiesis. The principal mechanism of hepcidin is its inhibition of cellular iron efflux, blocking the effect of

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the transport protein, ferroportin; under these conditions, macrophages, hepatocytes, and enterocytes retain iron (Atanasiu et al 2007; Ganz 2006). As iron is not released into the circulation, the availability to erythroid precursors is reduced. High hepcidin concentrations cause cellular iron overload, as occurs in hemochromatosis, and contribute to the typical pattern of chronic anemia referred as "functional iron deficiency." Roxadustat effects on hepcidin were studied in 6 Phase 1 studies and the Phase 2 and Phase 3 studies. Roxadustat was shown to cause a significant decrease in hepcidin levels from baseline in healthy subjects as well as patients with NDD CKD and DD CKD over a period of up to 24 weeks.

4.3.1.4. Serum Iron Markers

Roxadustat effects on iron utilization (iron status: serum iron, ferritin, TSAT, and soluble transferrin receptor) were studied in patients concomitantly treated with iron products in main Phase 3 studies. The data indicate that in patients with NDD CKD who did not receive ESA, levels of serum ferritin and TSAT initially decreased after the start of roxadustat treatment compared to placebo, then gradually increased to plateau around Week 20 and remained generally constant to Week 52. Serum iron levels decreased after the start of roxadustat treatment, then increased above the baseline in the roxadustat arm and were greater at each treatment visit compared with the placebo arm. Those data suggests that with a fall in hepcidin, ferritin is released from its sequestration. Iron is utilized during the period of anemia correction and then the stores rise (likely through the increased availability through intestinal absorption) during the period of maintenance. Similar findings were observed in patients with DD CKD.

4.3.2. Pharmacodynamic Markers of Safety

4.3.2.1. Heart Rate and Blood Pressure

Roxadustat treatment has been shown to produce a dose-dependent increase in heart rate in healthy subjects at doses greater than 2 mg/kg: a placebo-corrected heart rate increase of up to 9 to 10 beats per minute (bpm) at 8 to 12 h post-dose for the 2.75 mg/kg dose and 15 to 18 bpm at 6 to 12 h post-dose for the dose of 5 mg/kg. There was no clinically meaningful effect of roxadustat on blood pressure.

4.3.2.2. OT Intervals

A thorough QT study in healthy subjects was conducted using a therapeutic dose of 2.75 mg/kg (up to 280 mg) and a single supratherapeutic dose of 5 mg/kg (up to 510 mg) of roxadustat. There was no meaningful prolongation.

5. CLINICAL EFFICACY

5.1. Pivotal and Supportive Phase 3 NDD Studies

5.1.1. Study Design

The pivotal NDD studies were double-blind, placebo-controlled studies with a randomization scheme of 2:1 to roxadustat or placebo in Studies 060 and 608, and 1:1 in Study 001. The primary efficacy objective of these studies was to evaluate the efficacy of roxadustat in correcting anemia and maintaining Hb levels at 11 ± 1 g/dL for at least 52 weeks. The overall program was sized and was later extended up to 4 years to accumulate a sufficient number of adjudicated CV endpoints to evaluate CV safety.

In the pivotal NDD studies, given that the majority of patients with NDD CKD do not currently receive ESA treatment for their anemia, the studies were designed to use an oral placebo comparator in a double-blind study design to minimize bias and maintain clinical equipoise comparing the treatment of anemia with roxadustat to the lack of effective treatment for anemia which in essence patients with CKD (not requiring dialysis) are currently receiving. From a safety perspective, use of a placebo comparator is considered the gold standard to evaluate causality to treatment rather than comparing against an active comparator from a different drug class.

Key study design features are summarized in Table 18.

Table 18: Overview of Key Design Features of Pivotal and Supportive Phase 3
Studies in Patients with NDD CKD

Key design	Placebo-con	ESA-controlled Supportive Phase 3 NDD Study			
features	Study 608 Study 060 Study		Study 001	Study 610	
Number of Patients	594	922	2761	616	
CKD stage	III-V	III-V	III-V	III-V	
Randomization	2:1	2:1	1:1	1:1	
Planned Treatment Duration (weeks)	52–104	52 – up to 4 years	52 – up to 4 years	104	
Baseline eGFR (mL/min/1.73 m ²)	< 60	< 60	< 60	< 60	
Baseline Hb (g/dL)	≤ 10.0	≤ 10.0	< 10.0	≤ 10.5	
Hb Aim (g/dL) – Correction Period	\geq 11.0 and \geq 1.0 from baseline	≥ 11.0 and ≥ 1.0 from baseline	11.0 ± 1.0†	\geq 11.0 and \geq 1.0 from baseline	
Hb Aim (g/dL) – Maintenance Period	10.0–12.0	10.0–12.0	10.0–12.0	10.0–12.0	

Abbreviations: CKD=chronic kidney disease, eGFR=estimated glomerular filtration rate, ESA=erythropoiesis-stimulating agent; Hb=hemoglobin, NDD=non-dialysis-dependent.

[†]Treatment period was not split between correction and maintenance periods.

5.1.1.1. Efficacy Endpoints in Pivotal NDD Studies

5.1.1.1.1. Primary Efficacy Endpoint

The key primary efficacy endpoint for all 3 studies was the mean change in Hb (g/dL) from baseline to mean over Weeks 28 to 52 regardless of rescue therapy.

5.1.1.1.2. Selected Secondary Efficacy Endpoints

The secondary efficacy endpoints included:

- Proportion (%) of patients who achieved a Hb response at 2 consecutive visits during the first 24 weeks of treatment without rescue therapy (ie, RBC transfusion, ESA or IV iron)
 - A Hb response is defined as a Hb \geq 11.0 g/dL and a Hb increase from baseline by \geq 1.0 g/dL in patients with baseline Hb > 8.0 g/dL, or a Hb increase from baseline by \geq 2.0 g/dL in a patient with baseline Hb \leq 8.0 g/dL.
- Mean change from baseline in Hb to mean over Week 28 to 36 without rescue therapy within 6 weeks prior to and during this 8-week evaluation period
- Proportion (%) of patients with Hb level ≥ 10 g/dL averaged over Week 28 to 36 without use of rescue therapy within 6 weeks prior to and during these 8-week evaluation periods
- Mean change from baseline in Hb to mean over Week 28 to 52 regardless of rescue therapy in patients with baseline hsCRP>ULN
- Mean change from baseline in LDL cholesterol to mean over Week 12 to 28
- Time to (and % of patients who received) first rescue therapy (composite of blood/RBC transfusion, ESA use, and IV iron) over the first 52 weeks of treatment
- Time to first blood/RBC transfusion over the first 52 weeks of treatment

5.1.1.1.3. Exploratory Efficacy Endpoints

- Serum Hepcidin change from Baseline to Week 24 in patients with NDD CKD
- Serum Iron Markers: Assessment of mean serum iron, ferritin, and TSAT over time as indicators of iron status in patients with NDD CKD

5.1.1.2. Patient Eligibility Criteria in Pivotal NDD Studies

All eligible patients in the pivotal Phase 3 program were adult patients with CKD anemia. Patient eligibility for all studies specified a Hb threshold as an important inclusion criterion as well as threshold criteria for minimal iron stores. Patients with folate or B12 deficiencies and other known causes of anemia were excluded.

In the 3 pivotal NDD studies (Studies 060, 608 and 001), patients were to have CKD Stage 3–5, an eGFR < 60 mL/min/1.73 m² and Hb < 10.0 g/dL at baseline. Study 060 and 608 excluded patients with ESA use within 12 weeks prior to randomization; in Study 001, the exclusion period was 6 weeks.

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All patients were required to have an average baseline Hb \leq 10.0 g/dL based on the 2 or 3 most recent Hb values obtained during the screening period, except Study 610 which allowed an average Hb \leq 10.5 g/dL. Baseline ferritin was required to be \geq 30 ng/mL (for Studies 608 and 060), \geq 50 ng/mL (for Study 001) or \geq 100 ng/mL (Study 610). Patients could not have received any ESA treatment within 12 weeks (Studies 060 or 608) or 6 weeks (Study 001) in the global Phase 3 studies.

5.1.1.3. Statistical Analyses in Pivotal NDD Studies

5.1.1.3.1. Comparisons of Results from Individual Studies

The observed results and estimates of treatment effect (eg, mean Hb change from baseline on roxadustat and placebo), as well as CIs and p-values from the treatment comparison analyses for each study were presented side by side to demonstrate substantial evidence of effectiveness for each indication.

5.1.1.3.2. Pooled Analyses

The pooled analyses for the primary endpoint were performed on the ITT Population (which included all randomized patients). The rest of pooled analyses were performed on the Full Analysis Set (FAS) population (which included all randomized/enrolled patients who received at least one dose of study drug and had at least one post-dose Hb assessment). Overall analyses of dose safety were based on the Safety Analysis Set population (which included any randomized/enrolled patient with at least one dose of study drug). For the overall and subgroup analyses of the primary endpoint, the change from baseline Hb data from the multiple imputation (MI) datasets in each study were pooled and analyzed. The analysis model had terms for treatment, study, study*treatment interaction term and common randomization stratification factors as appropriate. Then, using the PROC MIANALYZE approach to summarize the results over the imputations. In the placebo-controlled global Phase 3 NDD CKD studies, the FDA primary efficacy endpoint of change from baseline in Hb to mean over Weeks 28 to 52 was evaluated using the MI Analysis of Covariance model (MI ANCOVA]), and superiority was established if p < 0.05 in Studies 060, 001, and 608. The pooled analysis methods for the same endpoints were analyzed following the same primary analysis method as specified in the individual study.

In general, the missing data handling for the analyses in the pooled dataset followed the same approach as for the primary analysis described for the individual studies. For example, the missing data for the change from baseline in Hb primary endpoint were imputed using the PROC MI procedure.

5.1.2. Demographic and Baseline Characteristics in Pivotal NDD Studies

Demographics and baseline characteristics in the ITT Population are provided in Table 19.

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 Table 19:
 NDD Studies: Demographic and Baseline Characteristics

	NDD Population							
	Study 608		Study 060		Study 001		Pooled NDD Population	
	Roxa (N=391)	Placebo (N=203)	Roxa (N=616)	Placebo (N=306)	Roxa (N=1384)	Placebo (N=1377)	Roxa (N=2391)	Placebo (N=1886)
Age, years								
Mean (SD)	60.6 (13.5)	61.7 (13.8)	64.9 (12.6)	64.8 (13.2)	60.9 (14.7)	62.4 (14.1)	61.9 (14.08)	62.7 (13.98)
Male, n (%)	169 (43.2)	99 (48.8)	241 (39.1)	130 (42.5)	564 (40.8)	603 (43.8)	974 (40.7)	832 (44.1)
Race, n (%)								
White	335 (85.7)	182 (89.7)	176 (28.6)	99 (32.4)	623 (45.0)	611 (44.4)	1134 (47.4)	892 (47.3)
Black/African American	10 (2.6)	3 (1.5)	76 (12.3)	28 (9.2)	112 (8.1)	115 (8.4)	198 (8.3)	146 (7.7)
Asian	9 (2.3)	0	310 (50.3)	151 (49.3)	544 (39.3)	538 (39.1)	863 (36.1)	689 (36.5)
Other	37 (9.5)	18 (8.9)	46 (7.5)	23 (7.5)	81 (5.9)	82 (5.0)	196 (8.2)	159 (8.4)
Region, n (%)								
Ex-U.S.	391 (100)	203 (100)	209 (33.9)	101 (33.0)	1041 (75.2)	1037 (75.3)	1839 (76.9)	1445 (76.6)
U.S.	0	0	407 (66.1)	205 (67.0)	343 (24.8)	340 (24.7)	552 (23.1)	441 (23.4)
BMI, kg/m ²								
Mean (SD)	27.06 (5.5)	27.63 (5.5)	27.4 (6.3)	27.3 (6.0)	26.58 (6.0)	26.85 (6.1)	26.9 (6.0)	27.0 (6.0)
Hb, g/dL								
Mean (SD)	9.1 (0.8)	9.1 (0.7)	9.1 (0.8)	9.1 (0.7)	9.1 (0.7)	9.1 (0.7)	9.1 (0.7)	9.1 (0.7)
hsCRP, n (%)								
≤ULN	245 (63.1)	135 (66.8)	457 (74.2)	223 (72.9)	520 (37.6)	497 (36.1)	1222 (51.1)	855 (45.3)
≥ULN	143 (36.9)	67 (33.2)	156 (25.3)	81 (26.5)	227 (16.4)	209 (15.2)	526 (22.0)	357 (18.9)
Baseline eGFR (ml/min/1.73 m²)								

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	NDD Population							
	Study 608		Study 060		Study 001		Pooled NDD Population	
	Roxa (N=391)	Placebo (N=203)	Roxa (N=616)	Placebo (N=306)	Roxa (N=1384)	Placebo (N=1377)	Roxa (N=2391)	Placebo (N=1886)
Mean (SD)	16.5 (10.2)	17.2 (11.7)	21.9 (11.5)	22.4 (11.4)	19.7 (11.7)	20.0 (11.7)	19.7 (11.6)	20.0 (11.8)
< 10	119 (30.4)	57 (28.1)	71 (11.5)	19 (6.2)	291 (21.0)	283 (20.6)	481 (20.1)	359 (19.0)
10 - < 15	102 (26.1)	61 (30.0)	124 (20.1)	76 (24.8)	300 (21.7)	315 (22.9)	526 (22.0)	452 (24.0)
15 - < 30	128 (32.7)	58 (28.6)	292 (47.4)	146 (47.7)	534 (38.6)	520 (37.8)	954 (39.9)	724 (38.4)
≥ 30	42 (10.7)	26 (12.8)	129 (20.9)	65 (21.2)	259 (18.7)	259 (18.8)	430 (18.0)	351 (18.6)
Iron Repletion Status, n(%)								
Ferritin < 100 ng/ml and TSAT < 20%	187 (47.8)	94 (46.3)	241 (39.1)	134 (43.8)	575 (41.5)	578 (42.0)	956 (40.0)	755 (40.0)
Ferritin ≥ 100 ng/ml or TSAT ≥ 20%	204 (52.2)	109 (53.7)	373 (60.6)	170 (55.6)	809 (58.5)	799 (58.0)	1433 (59.9)	1127 (59.8)
Diabetes Mellitus, n(%)	131 (33.5)	76 (37.4)	395 (64.6)	199 (65.2)	793 (57.3)	807 (58.6)	1337 (55.9)	1096 (58.1)

Abbreviations: BMI=body mass index; eGFR=estimated glomerular filtration rate; Hb=hemoglobin; hsCRP=high-sensitivity C-reactive protein; Max=maximum; min=Minimum; NDD=non-dialysis-dependent; Roxa=roxadustat; SD=standard deviation; TSAT=transferrin saturation; ULN=upper limit of normal; US=United States of America. Note: Intent-to-treat analysis set.

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5.1.3. Efficacy Results in Pivotal NDD Studies

5.1.3.1. Primary Efficacy Endpoint Results

The primary efficacy endpoint results from the pooled NDD studies are shown in Table 20. Roxadustat treatment of patients with NDD CKD met the pre-specified primary efficacy endpoint with a statistically significant (p < 0.001) improvement in mean Hb levels regardless of rescue therapy in the pooled ITT Population compared to the placebo.

Table 20: NDD Studies: Mean Change in Hb from Baseline to Mean Over Weeks 28 to 52 Regardless of Rescue Therapy

Hb (g/dL)	Stud	y 608	Stud	y 060	Stud	y 001	NDD	Pool
	Roxa n=391	Placebo n=203	Roxa n=616	Placebo n=306	Roxa n=1384	Placebo n=1377	Roxa n=2391	Placebo n=1886
Baseline Hb							•	
n	391	203	616	306	1384	1376	2391	1886
Mean (SD)	9.08 (0.76)	9.10 (0.72)	9.10 (0.75)	9.09 (0.69)	9.11 (0.733)	9.10 (0.742)	9.10 (0.743)	9.10 (0.732)
Average Hb in Weeks 28 to 52								
n	312	146	616	306	NA	NA	2391	1886
Mean (SD)	11.16 (0.84)	9.60 (1.03)	11.10 (0.70)	9.25 (1.06)	NA	NA	10.95 (0.758)	9.23 (1.111)
ANCOVA with Multiple Imputa	ations						•	
LSMean Change (SE)	1.99	0.30	2.02 (0.036)	0.17 (0.051)	1.75 (0.033)	0.40 (0.034)	1.94 (0.022)	0.22 (0.030)
95% CI	(1.82, 2.16)	(0.09, 0.51)	(1.947, 2.089)	(0.066, 0.267)	(1.68, 1.81)	(0.33, 0.47)	(1.898, 1.983)	(0.159, 0.276)
LSMean Difference (SE)	1.6	592	1.85 (0.059)	1.35 (0.041)		1.72 (0.036)	
95% CI	(1.52,	1.86)	(1.735,	, 1.967)	(1.27, 1.43)		(1.653, 1.794)	
p-value	< 0.	001	< 0	.001	< 0.001		< 0.001	

Abbreviations: ANCOVA=analysis of covariance; CI=confidence interval; Hb=hemoglobin; ITT=intent-to-treat; LSMean=least squares mean; Max=maximum; Min=minimum; NDD=non-dialysis-dependent; Roxa=roxadustat; SD=standard deviation; SE=standard error.

Note: ITT

5.1.3.2. Selected Secondary Efficacy Endpoint Results

5.1.3.2.1. Proportion of Patients Achieving Hb Response During the First 24 Weeks of Treatment Without Rescue Therapy

Table 21 shows the proportion of patients achieving a Hb response as defined in 5.1.1.1.2. In the pooled FAS population at the end of the 24-week treatment period, 80.2% of roxadustat-treated patients achieved a Hb response compared to 8.7% of placebo-treated patients; the difference in Hb response was statistically significant at p < 0.001.

Table 21: NDD Studies: Proportion of Patients Who Achieved Hb Response During the First 24 Weeks of Treatment, Censoring for Rescue Therapy

	Stud	y 608	Study	y 060	Stud	y 001	NDD	Pool	
	Roxa n=389	Placebo n=203	Roxa n=608	Placebo n=305	Roxa n=1371	Placebo n=1357	Roxa n=2368	Placebo n=1865	
Patients Who Achieved Hb Response (%)	308 (79.2)	20 (9.9)	523 (86.0)	20 (6.6)	1055 (77.0)	115 (8.5)	1899 (80.2)	163 (8.7)	
95% CI ^a	(74.8, 83.1)	(6.1, 14.8)	(83.0, 88.7)	(4.1, 9.9)	NR	NR	(78.5, 81.8)	(7.5, 10.1)	
Treatment Response Rate Difference (95% CI)		.7, 75.1)	79.5 (75.5	79.5 (75.55, 83.38)		, 10.89) ^b	71.5 (69.40, 73.51)		
p-value	< 0.	001	< 0.	< 0.001		< 0.001		< 0.001	

Abbreviations: CI=confidence interval; NDD=non-dialysis-dependent; NR=not reported; Roxa=roxadustat.

Note: Full analysis set.

5.1.3.2.2. Proportion of Patients with Hb \geq 10 g/dL Without Rescue Therapy

As shown in Table 22, a significantly higher proportion of patients from the roxadustat group (72.8%) achieved a mean Hb level of ≥ 10.0 g/dL averaged over weeks 28 to 36 compared to the placebo group (18.9%; p < 0.001).

^a 95% CI of response rate for each treatment group is based on the exact method of Clopper-Pearson.

^b Study 001 reported relative risk.

Table 22: NDD Studies: Proportion of Patients with Hb ≥ 10.0 g/dL Averaged Over Weeks 28 to 36 Censoring for Rescue Therapy

	Stud	y 608	Stud	y 060	Study	y 001 [†]	NDD	Pool	
	Roxa n=389	Placebo n=203	Roxa n=608	Placebo n=305	Roxa n=1384	Placebo n=1377	Roxa n=2368	Placebo n=1865	
n (%)	NA	NA	467 (76.8)	56 (18.4)	(82)	(33)	1725 (72.8)	352 (18.9)	
95% CI ^a	NA	NA	(73.2, 80.1)	(14.2, 23.2)	NA	NA	(71.0, 74.6)	(17.1, 20.7)	
Treatment Response Rate Difference (95% CI)	N	Ā	58.4 (52.	58.4 (52.96, 63.94)		50 (47, 52)†		45, 56.49)	
Roxa/Placebo Odds Ratio (95% CI) ^b	N	Ā	15.47 (10	.79, 22.19)	N	ÍΑ	12.27 (10	50, 14.34)	
p-value	N	NA		< 0.001		< 0.001		< 0.001	

Abbreviations: ANCOVA=analysis of covariance; CI=confidence interval; eGFR=estimated glomerular filtration rate; Hb=hemoglobin; NA=not available (endpoint not analyzed); NDD=non-dialysis-dependent; Roxa=roxadustat; US=United States.

Note: Full analysis set.

5.1.3.2.3. Mean Change from Baseline in LDL Cholesterol

Patients treated with roxadustat had a 17% reduction in LDL cholesterol from baseline in the pooled NDD population compared to the placebo group (LSMean of the treatment difference [-19.8 mg/dL]) (p < 0.001) (Table 23).

^a the 95% CI of response rate for each treatment group is based on the exact method of Clopper-Pearson.

^b From Cochran-Mantel-Haenszel method adjusting for study, region (US, Europe, Other), baseline Hb (< 8 g/dL vs \geq 8 g/dL), baseline eGFR (< 30 vs \geq 30 mL/min/1.73 m²), and history of cardiovascular/ cerebrovascular/thromboembolic diseases (Yes vs No).

^{†:} in Study 001, this endpoint was defined as "proportion of total time of interpolated Hb (g/dL) values \geq 10 g/dL, from Weeks 28 to 52 analyzed by ANCOVA in the intent-to-treat set."

Table 23: NDD Studies: Mean Change from Baseline in LDL Cholesterol to Mean Over Weeks 12 to 28

	Stud	y 608	Stud	y 060	Study	v 001 †	NDD	Pool
LDL (mg/dL)	Roxa n=389	Placebo n=203	Roxa n=608	Placebo n=305	Roxa n=1384	Placebo n=1377	Roxa n=2368	Placebo n=1865
Baseline LDL ^a (1	mg/dL)							
n	389	203	608	305	1272	1283	2256	1771
Mean (SD)	115.43 (49.69)	111.49 (44.16)	97.74 (39.09)	96.39 (40.06)	94.35 (43.39)	92.41 (41.98)	98.97 (44.151)	95.53 (42.401)
Median	108.28	105.18	92.00	89.00	86.62	87.00	92.00	89.33
Min, Max	26.30, 369.30	15.85, 259.86	15.0, 363.0	10.0, 252.0	1.16, 356.54	5.41, 465.97	1.2, 369.3	5.4, 466.0
Average LDL in	Weeks 12–2	8 (mg/dL)						
n	342	185	564	269	1233	1214	1994	1430
Mean (SD)	93.27 (35.34)	117.60 (47.87)	79.25 (29.62)	96.84 (37.69)	81.14 (39.28)	93.98 (43.51)	81.83 (36.187)	97.55 (43.793)
Median	88.67	112.80	74.83	88.67	72.31	88.17	75.00	90.22
Min, Max	21.27, 220.03	20.88, 336.43	14.3, 230.0	14.0, 249.0	10.1, 298.1	14.0, 491.1	10.1, 298.1	14.0, 491.1
ANCOVA b								
LSMean (SE)	-25.14	1.97	-18.41 (1.45)	-1.15 (1.82)	-14.69 (1.08)	-0.77 (1.04)	-17.26 (0.735)	2.57 (0.969)
95% CI	(-29.39, -20.88)	(-3.09, 6.96)	(-21.27, -15.56)	(-4.73, 2.42)	(-16.63, -12.37)	(-2.71, 1.55)	(-18.70, - 15.82)	(0.67, 4.47)
LSMean Difference (SE)	-27.	-27.11 ‡		-17.26 (1.73)		-13.92 (1.28)		(1.186)
95% CI	(-32.10	, -22.04)	(-20.65, -13.87)		(-16.24, -11.21)		(-22.16, -17.51)	
p-value	< 0	.001	< 0.	.001	< 0	.001	< 0	.001

Abbreviations: ANCOVA=analysis of covariance; CI=confidence interval; eGFR=estimated glomerular filtration rate; FAS=full analysis set; Hb=hemoglobin; ITT=intent-to-treat; LDL=low-density lipoprotein; LSMean=least squares mean; Max=maximum; Min=minimum; NDD=non-dialysis-dependent; Roxa=roxadustat; SD=standard deviation; SE=standard error; US=United States.

Note: Full analysis set.

5.1.3.2.4. Proportion of Patients Receiving Any Rescue Therapy During the First **52** Weeks of Treatment

The proportion of patients who received any rescue therapy (RBC transfusion, ESA use, and IV iron) in the first 52 weeks of treatment was significantly lower in the roxadustat group (8.9%) than in the placebo group (31.1%; p < 0.001) (Table 24).

a: Baseline is defined as the last available value prior to the first dose of study treatment.

b: Treatment comparison was made using an ANCOVA model with baseline Hb, baseline eGFR, baseline LDL as covariates, and study, treatment, study-by-treatment interaction, history of cardiovascular/cerebrovascular/thromboembolic diseases (Yes vs No) and region (US, Europe, Other) as fixed effects.

^{†:} in Study 001, this endpoint was defined as mean change in LDL (mmol/L) from baseline to Week 24 analyzed by ANCOVA in ITT set.

^{‡:} No SE available.

Table 24: NDD Studies: Patients Receiving Rescue Therapy in the First 52 Weeks

Rescue Therapy	Study	y 608‡	Stud	y 060	Study	7 001 †	NDD	Pool
	Roxa n=389	Placebo n=203	Roxa n=608	Placebo n=305	Roxa n=1384	Placebo n =1376	Roxa n=2368	Placebo n=1865
Patients with events ^a , n (%)	64 (16.5)	93 (45.8)	54 (8.9)	88 (28.9)	254 (18.35)	574 (41.72)	211 (8.9)	580 (31.1)
Patients censored ^b , n (%)	NA	NA	554 (91.1)	217 (71.1)	1130 (81.65)	802 (58.28)	2157 (91.1)	1285 (68.9)
Treatment Effect (roxa-placebo) HR ^c	0.2	238	0.	0.19		26	0.	19
95% CI ^c	(0.17,	, 0.33)	(0.138,	, 0.276)	(0.23,	0.31)	(0.164,	0.226)
p-value ^c	< 0.	.001	< 0.	.001	< 0.	.001	< 0.	.001
Total PEY d	438.5	155.9	527.3	230.9	2134.88	1443.49	2031.8	1414.3
Incidence rate of events (per 100 PY)	14.6	59.6	10.2	38.1	11.90	39.76	10.4	41.0

Abbreviations: CI=confidence interval; eGFR=estimated glomerular filtration rate; EOT=end of treatment;

Note: Full analysis set.

5.1.3.2.5. Proportion of Patients Receiving RBC Transfusions During the First **52** Weeks of Treatment

The proportion of patients who received RBC transfusion in the first 52 weeks of treatment was also significantly lower in the roxadustat group (5.2%) than in the placebo group (15.4%; p < 0.001) (Table 25).

ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; HR=hazard ratio; IV=intravenous(ly); NA=not available;

NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PEY=patient exposure year; RBC=red blood cell; Roxa=roxadustat; US=United States.

a Rescue therapy: Any use of RBC transfusion, ESA, or IV iron.

b Patients with no event were censored at the date of minimum (last dose date, first dose date + 364 days, last visit date, death date).

c From a Cox Proportional hazards model adjusting for baseline Hb, baseline eGFR, study, treatment, region (US, Europe, Other), and history of cardiovascular/cerebrovascular/thromboembolic diseases (Yes vs No).

d: Total PEY was calculated as minimum (364 days, last dose date - first dose date +1).

^{†:} Endpoint was evaluated in the safety emergent period up to OT+28 in Study 001

^{‡:} Endpoint was evaluated in the efficacy emergent period (date of first dose intake up to 7 days after the date of last dose or EOT visit, whichever occurs first) in Study 608.

Table 25: NDD Studies: Patients Receiving RBC Transfusions in the First 52 Weeks

	Stud	y 608‡	Stud	y 060	Study	y 001 [†]	NDD	Pool
RBC Transfusion	Roxa n=389	Placebo n=203	Roxa n=608	Placebo n=305	Roxa n=1384	Placebo n=1376	Roxa n=2368	Placebo n=1865
Patients with events ^a	33	39	34	47	176	320	124	288
n (%)	(8.5)	(19.2)	(5.6)	(15.4)	(12.72)	(23.26)	(5.2)	(15.4)
Patients censored ^b n (%)	NA	NA	574 (94.4)	258 (84.6)	1208 (87.28)	1056 (76.74)	2244 (94.8)	1577 (84.6)
Treatment effect (Roxaplacebo) HR ^c	0.	343	0.	26	0.	37	0.2	26
95% CI ^c	(0.21	, 0.55)	(0.165,	, 0.406)	(0.30,	0.44)	(0.206,	0.318)
p-value ^c	< 0.001 ((nominal*)	< 0.001 (1	nominal*)	< 0.	.001	< 0.	001
Total PEY d	455.2	181.0	527.3	230.9	2206.74	1631.69	2031.8	1414.3
Incidence rate of events (per 100 PY)	7.2	21.5	6.4	20.4	7.98	19.61	6.1	20.4

Abbreviations: CI=confidence interval; eGFR=estimated glomerular filtration rate; EOT=end of treatment; Hb=hemoglobin; HR=hazard ratio; NA=not available; NDD=non-dialysis-dependent; NE=not estimable; OT+28=on-treatment plus 28 days; PEY=patient exposure year; RBC=red blood cell; Roxa=roxadustat; US=United States.

Note: Full analysis set.

One additional study in patients with NDD CKD comparing roxadustat to darbepoetin alfa was performed (Study 610). While Study 610 cannot be pooled with the 3 placebocontrolled studies in NDD due to the different comparator arms, a description of the results can be found in Section 1.3.4.

5.2. Pivotal and Supportive Phase 3 DD Studies

5.2.1. Study Design

The pivotal DD studies were open label with EPO as comparator with a randomization scheme of 1:1 to roxadustat or EPO (Table 26). The primary efficacy objective of these studies was to evaluate the efficacy of roxadustat in correcting anemia and maintaining Hb levels at 11±1 g/dL for at least 52 weeks. For the pivotal DD studies, a single ESA, EPO, was selected as the comparator to allow the comparison to only one agent and given that it is the standard of care treatment for anemia in this patient population. Because of its use of 2

^{*:} In Study 608 and Study 060, this endpoint fell below an endpoint in the hierarchical testing order that did not reach statistical significance and thus was considered nominal.

a Rescue therapy: Any use of RBC.

b Patients with no event were censored at the date of minimum (last dose date, first dose date + 364 days, last visit date, death date).

c: From a stratified Cox Proportional hazards model adjusting for baseline Hb, baseline eGFR, and treatment, stratified by study, region (US, Europe, Other), and history of cardiovascular/cerebrovascular/thromboembolic diseases (Yes vs No).

d: Total PEY was calculated as minimum (364 days, last dose date - first dose date +1).

^{‡:} Endpoint was evaluated in the efficacy emergent period (date of first dose intake up to 7 days after the date of last dose or EOT visit, whichever occurs first) in Study 608.

^{†:} Endpoint was evaluated in the safety emergent period up to OT+28 in Study 001.

comparators (EPO and darbepoetin alfa), Study 613 is not able to be pooled with the other 3 studies and is presented as supportive of efficacy.

Table 26: Overview of Key Design Features of Pivotal and Supportive Phase 3 Studies in Patients with DD CKD

	Epoetin Alfa-co	ntrolled Pivotal Ph	ase 3 DD Studies	ESA-controlled Supportive Phase 3 DD Study
Design Features	Study 063	Study 064	Study 002	Study 613
Region	Global	US	Global	Europe
Number of patients	1043	741	2106	836
ESA Control	Epoetin Alfa	Epoetin Alfa	Epoetin Alfa	Epoetin Alfa/Darbepoetin Alfa
Planned Treatment Duration (weeks)	up to 4 years	up to 4 years	up to 4 years	52–104
Dialysis Status	ID	SDD and ID	SDD and ID	SDD
Baseline Hb (g/dL)	≤ 10.0	9.0†–12.0	< 10.0‡, < 12.0	9.5–12.0
Hb Correction or ESA Conversion	Correction	Conversion	Correction and Conversion	Conversion
Hb Aim (g/dL) – Maintenance Period	10.0–12.0	10.0–12.0	10.0–12.0	10.0–12.0

Abbreviations: CKD=chronic kidney disease; DD=dialysis-dependent; ESA=erythropoieses-stimulating agent; ESRD=end-stage renal disease; Hb=hemoglobin; HD=hemodialysis; ID=incident dialysis; OL=open-label; SDD=stable dialysis-dependent; US=United States.

Note: Stable dialysis comprises the initiation of dialysis ≥ 4 months at the time of randomization. Incident dialysis comprises the initiation of dialysis ≥ 2 weeks but ≤ 4 months at the time of randomization.

5.2.1.1. Efficacy Endpoints in Pivotal Studies

5.2.1.1.1. Primary Efficacy Endpoint

The key primary efficacy endpoint for all global Phase 3 DD CKD studies was the mean change in Hb (g/dL) from baseline to mean over Weeks 28 to 52 regardless of rescue therapy.

5.2.1.1.2. Selected Secondary Efficacy Endpoints

The key secondary efficacy endpoints were:

- Mean change in Hb from baseline to mean over Week 28 to 36 without rescue therapy within 6 weeks prior to and during this 8-week evaluation period
- Proportion (%) of patients with Hb level averaged ≥ 10 g/dL over Week 28 to 36 without use of rescue therapy within 6 weeks prior to and during these 8-week evaluation periods

[†]≥ 8.5 g/dL for ID patients.

[‡]For patients not on ESA treatment.

Other secondary efficacy endpoints included:

- Hb change from baseline to the average in patients with DD CKD with baseline hsCRP > ULN between the pooled DD population and its constituent study populations.
- Mean LDL cholesterol changes from baseline to mean over Weeks 12 to 28
- Average monthly IV iron use over Weeks 28 to 52
- Proportion of patients who received RBC transfusion during treatment

5.2.1.1.3. Exploratory Efficacy Endpoints

- Serum Hepcidin change from Baseline to Week 24 in patients with DD CKD.
- Serum Iron Markers: Assessment of mean serum iron, ferritin, and TSAT over time as indicators of iron status in pooled FAS ID and SDD populations.

5.2.1.2. Patient Eligibility Criteria in Pivotal DD Studies

Adult male and female patients with CKD with anemia on hemodialysis or peritoneal dialysis with a Hb threshold as an inclusion criterion were eligible to participate. The ID and SDD populations were defined as patients who have been on dialysis for \leq 4 months or > 4 months, respectively, at the time of randomization. Studies 064 and 002 had mostly stable dialysis patients and some ID patients. Study 063 consisted of only ID patients that had to be on dialysis for \leq 4 months at the time of randomization. All patients in Study 063 were required to have an average baseline Hb < 10.0 g/dL. Study 063 excluded patients who had received more than 3 weeks of ESA treatment within 12 weeks prior to randomization. Study 064 required patients to have an average baseline Hb of 9.0–12.0 g/dL for stable dialysis patients and have been receiving IV or subcutaneous ESA (epoetin, darbepoetin, or methoxy polyethylene glycol-epoetin beta [Mircera®]) for \geq 8 weeks prior to randomization, whereas required baseline Hb \geq 8.5 g/dL for ID patients who have been on ESA for \geq 4 weeks prior to screening. Study 002 required patients with baseline Hb < 12 g/dL for patients treated with ESA previously and with baseline Hb < 10 g/dL for ESA-naïve patients.

5.2.1.3. Statistical Analyses in Pivotal DD Studies

The observed results and estimates of treatment effect (eg, mean Hb change from baseline on roxadustat and active control), as well as CIs from the treatment comparison analyses for each study were presented side by side to demonstrate substantial evidence of effectiveness. Similar as the pooled analyses performed in NDD population, the pooled analyses for the US primary endpoint in DD population were performed on the ITT Population. In the ESA-controlled global Phase 3 DD CKD studies, the FDA primary efficacy endpoint of change from baseline in Hb to mean over Weeks 28 to 52 was evaluated using MI ANCOVA with a non-inferiority margin of -0.75 g/dL. In general, the pooled analysis methods for the same endpoints were analyzed following the same primary analysis method as specified in the individual study. The missing data handling for the analyses in the pooled dataset followed the same approach for the primary analysis described for the individual studies.

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5.2.2. Demographic and Baseline Characteristics in Pivotal DD Studies

Demographics and baseline characteristics in the ITT Population are provided in Table 27.

Table 27: DD Studies: Demographic and Baseline Characteristics

				DD P	Population			
	Stud	ly 063	Stud	ly 064	Stud	ly 002	Pooled DD	Population
	Roxa (N=522)	Epoetin Alfa (N=521)	Roxa (N=370)	Epoetin Alfa (N=371)	Roxa (N=1051)	Epoetin Alfa (N=1055)	Roxa (N=1943)	Epoetin Alfa (N=1947)
Age, years								
Mean (SD)	53.8 (14.7)	54.3 (14.6)	57.6 (13.6)	58.4 (13.3)	53.5 (15.3)	54.5 (15.0)	54.3 (14.92)	55.2 (14.64)
Min, Max	19, 87	18, 92	22, 92	23, 88	18, 93	20, 94	18, 93	18, 94
Male, n (%)	309 (59.2)	307 (58.9)	187 (50.5)	215 (58.0)	625 (59.5)	626 (59.3)	1121 (57.7)	1148 (59.0)
Race, n (%)								
White	415 (79.5)	400 (76.8)	165 (44.6)	184 (49.6)	597 (56.8)	598 (56.7)	1177 (60.6)	1182 (60.7)
Black/African American	44 (8.4)	50 (9.6)	158 (42.7)	156 (42.0)	148 (14.1)	158 (15.0)	350 (18.0)	364 (18.7)
Asian	43 (8.2)	51 (9.8)	21 (5.7)	15 (4.0)	208 (19.8)	198 (18.8)	272 (14.0)	264 (13.6)
Other	19 (3.6)	16 (3.1)	15 (4.1)	6 (1.6)	43 (4.1)	36 (3.4)	144 (7.4)	137 (7.0)
Region, n (%)								
Ex-U.S.	395 (75.7)	396 (76.0)	0	0	666 (63.4)	664 (62.9)	1061 (54.6)	1060 (54.4)
U.S.	127 (24.3)	125 (24.0)	370 (100)	371 (100)	385 (36.6)	391 (37.1)	882 (45.4)	887 (45.6)
BMI, kg/m ^{2b}								
Mean (SD)	26.73 (5.8)	27.01 (6.0)	30.2 (7.4)	30.5 (7.5)	27.0 (6.8)	26.9 (6.4)	27.55 (6.77)	27.63 (6.66)
Min, Max	16.5, 47.7	15.2, 56.8	15.6, 58	17.3, 60.9	15.9, 64.9	14.7, 57.0	15.6, 64.9	14.7, 60.9
Hb, g/dL								
Mean (SD)	8.4 (1.0)	8.5 (1.0)	10.3 (0.7)	10.3 (0.7)	10.0 (1.2)	10.0 (1.2)	9.6 (1.3)	9.7 (1.3)
Min, Max	5.3, 10.2	5.0, 10.3	(8.4, 11.9)	(8.6, 12.0)	4.3, 12.0	5.4, 12.2	4.3, 12.0	5.0, 12.2
hsCRP, n (%)								
≤ULN	289 (55.4)	289 (55.5)	178 (48.1)	192 (51.8)	421 (40.1)	427 (40.5)	889 (45.8)	912 (46.8)

				DD F	Population			
	Stud	y 063	Stud	y 064	Stud	ly 002	Pooled DD	Population
	Roxa (N=522)	Epoetin Alfa (N=521)	Roxa (N=370)	Epoetin Alfa (N=371)	Roxa (N=1051)	Epoetin Alfa (N=1055)	Roxa (N=1943)	Epoetin Alfa (N=1947)
≥ULN	228 (43.7)	226 (43.4)	189 (51.1)	177 (47.7)	303 (28.8)	311 (29.5)	723 (37.2)	722 (37.1)
Ferritin, ng/mL								
Mean (SD)	441.4 (337.0)	437.4 (311.4)	1002.2 (459.1)	960.8 (414.8)	NA	NA	610.57 (467.8)	603.24 (467.0)
Min, Max	33.0, 2852.8	38.9, 1896.0	107.3, 5184.5	92.3, 3229.0)	NA	NA	17.5, 5185.5	10.7, 4577.0
Hb n (%)								
\leq 8.0 g/dL or \leq 10 g/dL ^a	166 (31.8)	157 (30.1)	230 (62.2)	235 (63.3)	448 (42.6) a	435 (41.2) a	1083 (55.7) a	1058 (54.3) a
> 8.0 g/dL or > 10 g/dL a	356 (68.2)	364 (69.9)	140 (37.8)	136 (36.7)	603 (57.4) a	620 (58.8) a	860 (44.3)	889 (45.7)
TSAT (%) mean (SD)	27.02 (9.3)	27.56 (8.9)	33.6 (10.1)	33.6 (10.0)	NA	NA	33.03 (12.77)	32.66 (12.36)
ESA-Naïve (%)	93.7	93.8	0	0	0	0	29.0°	28.5 °
≤ 150 IU/kg/week, n(%)	NA	NA	298 (80.5)	301 (81.1)	NA	NA	1066 (54.9)°	1050 (54.1)°
> 150 IU/kg/week, n(%)	NA	NA	72 (19.5)	70 (18.9)	NA	NA	209 (10.8)°	233 (12.0) °
Diabetes n (%)	205 (39.3)	204 (39.2)	250 (67.5)	255 (68.8)	459 (43.7%)/	454 (43.0%)	915 (47.1)	915 (47.0)
Cardiovascular disease n (%)	141 (27.0)	149 (28.6)	140 (37.8)	134 (36.1)	372 (35.4)	383 (36.3)	047 (49 7) h	929 (47.7) ^b
Cerebrovascular Disease n (%)	77 (14.8)	79 (15.2)	56 (15.1)	53 (14.3)	305 (29.0)	304 (28.8)	947 (48.7) ^b	929 (47.7)
Peritoneal Dialysis	53 (10.2)	58 (11.1)	16 (4.3)	17 (4.6)	111 (10.6)	117 (11.1)	180 (9.3)	192 (9.9)

Abbreviations: BMI=body mass index; DD=dialysis-dependent; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; hsCRP=high-sensitivity C-reactive protein; Max=maximum; Min=minimum; Roxa=roxadustat; SD=standard deviation; TSAT=transferrin saturation; ULN=upper limit of normal; US=United States of America.

^a: Hb, n (%) in the Study 002 and pooled DD population were categorized by $< 10 \text{ vs} \ge 10 \text{ g/dL}$.

b: History of cardiac, cerebrovascular, or thromboembolic disease, n (%), were combined in the pooled DD population.

c: ESA use at baseline in the pooled DD population is the Safety Analysis Set defined as randomized patients who took any dose of study medication Note: Intent-to-treat analysis set.

5.2.3. Efficacy Results in Pivotal DD Studies

5.2.3.1. Primary Efficacy Endpoint Results

The pre-specified primary endpoint was met in the pooled DD studies. The effect including the 95% CI of roxadustat was within the pre-specified non-inferiority margin (-0.75 g/dL), thereby demonstrating non inferiority compared to EPO on mean change from baseline in Hb over Weeks 28 to 52 regardless of rescue therapy (ie, RBC transfusion and ESA) (Table 28).

Table 28: DD Studies: Mean Change in Hb from Baseline to Mean Over Weeks 28 to 52 Regardless of Rescue Therapy

	Stud	y 063	Stud	y 064	Stud	y 002	DD	Pool
Hb (g/dL)	Roxa n=522	EPO n=521	Roxa n=370	EPO n=371	Roxa n=1051	EPO n=1055	Roxa n=1943	EPO n=1947
Baseline Hb	•							
n	522	521	370	371	1051	1055	1943	1947
Mean (SD)	8.43 (1.044)	8.46 (0.964)	10.30 (0.661)	10.31 (0.656)	9.99 (1.195)	10.02 (1.235)	9.63 (1.300)	9.66 (1.301)
Median	8.60	8.60	10.29	10.33	10.20	10.30	9.80	9.80
Min, Max	5.3, 10.2	5.0, 10.3	8.4, 11.9	8.6, 12.0	4.3, 12.0	5.4, 12.2	4.3, 12.0	5.0, 12.2
Average Hb in W	eeks 28 to 52	(Observed	+ Imputed)					
n	522	521	370	371	NA	NA	1943	1947
Mean (SD)	11.00 (0.819)	10.83 (0.876)	10.69 (0.757)	10.22 (0.681)	NA	NA	10.85 (0.820)	10.65 (0.908)
Median	11.09	10.89	10.75	10.25	NA	NA	10.95	10.66
Min, Max	8.0, 13.5	6.8, 13.2	7.7, 13.2	7.3, 14.8	NA	NA	7.6, 13.5	6.8, 15.0
ANCOVA with M	Iultiple Impu	itations						
LSMean (SE)	2.38 (0.041)	2.20 (0.041)	0.28 (0.067)	-0.19 (0.063)	0.77 (0.041)	0.68 (0.040)	1.21 (0.023)	0.95 (0.022)
95% CI	(2.298, 2.461)	(2.115, 2.278)	(0.153, 0.414)	(-0.318, -0.071)	(0.69, 0.85)	(0.60, 0.76)	(1.167, 1.256)	(0.906, 0.992)
LSMean Difference (SE)	0.18 (0.053)		0.48 (0.058)		0.09 (0.044)		0.26 (0.032)	
95% CI	(0.079,	0.287)	(0.365,	0.591)	(0.01,	0.18)	(0.200,	, 0.325)

Abbreviations: ANCOVA=analysis of covariance; CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; Hb=hemoglobin; ITT=intent-to-treat analysis set; LSMean=least squares mean; Max=maximum; Min=minimum;

Roxa=roxadustat; SD=standard deviation; SE=standard error.

Note: Intent-to-treat analysis set.

5.2.3.2. Selected Secondary Efficacy Endpoints Results

5.2.3.2.1. Mean Change from Baseline to Mean Over Weeks 28 to 36 Without Rescue Therapy

Table 29 shows Hb response as mean change from baseline averaged over Week 28–36 without rescue therapy between pooled and its individual study populations.

Table 29: DD Studies: Hb Response with Roxadustat Compared with Epoetin Alfa Over Weeks 28 to 36 in DD Patient Censoring for Rescue Therapy

	Stud	y 063	Stud	y 064	Stud	y 002	DD	Pool
Hb (g/dL)	Roxa n=490	EPO n=468	Roxa n=334	EPO n=352	Roxa n=842	EPO n=869	Roxa n=1666	EPO n=1689
Baseline Hb ^a								
n	490	468	303	324	842	869	1666	1689
Mean (SD)	8.43 (1.043)	8.43 (0.963)	10.33 (0.639)	10.35 (0.614)	9.98	10.04	9.60 (1.312)	9.66 (1.303)
Median	8.60	8.56	10.30	10.33	NA	NA	9.73	9.80
Min, Max	5.3, 10.2	5.0, 10.3	8.8, 11.9	8.9, 12.0	NA	NA	4.3, 12.0	5.0, 12.2
Average Hb in We	eks 28–36							
n	433	418	263	293	NA	NA	1435	1500
Mean (SD)	11.13 (1.061)	10.94 (1.024)	10.89 (0.869)	10.33 (0.766)	NA	NA	10.96 (0.974)	10.71 (1.036)
Median	11.25	11.00	10.93	10.35	NA	NA	11.05	10.70
Min, Max	5.9, 13.8	7.4, 13.6	7.8, 13.0	7.6, 15.4	NA	NA	5.9, 13.8	5.0, 15.4
Mixed Model of Ro	epeated Mea	asures						
LSMean (SE)	2.59 (0.054)	2.39 (0.055)	0.63 (0.133)	0.09 (0.131)	0.88 (0.044)	0.74 (0.043)	1.32 (0.029)	1.03 (0.028)
95% CI	(2.483, 2.696)	(2.283, 2.500)	(0.373, 0.896)	(-0.169, 0.347)	NA	NA	(1.261, 1.375)	(0.975, 1.087)
LSMean Difference (SE)	0.20 (0	0.20 (0.076) ^b		0.55 (0.072) °		0.056) ^d	0.29 (0.041) e	
95% CI	(0.049	, 0.346)	(0.404,	0.687)	(0.03,	0.25)	(0.207,	, 0.366)

Abbreviations: CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; Hb=hemoglobin; LSMean=least squares mean; Max=maximum; Min=minimum; MMRM=mixed model of repeated measures; Roxa=roxadustat; SD=standard deviation; SE=standard error of the mean; US=United States.

Note: Hb values under the influence of a rescue therapy were censored up to 6 weeks in the analysis.

Note: Per Protocol Set

a: Baseline Hb is defined as the mean of up to 4 last central lab values prior to the first dose of study treatment.

b: In Study 063, treatment comparison was made using an MMRM with baseline Hb as covariate, and study, treatment, visit, visit-by-treatment interaction, study-by-treatment interaction, and history of cardiovascular/cerebrovascular/thromboembolic diseases (Yes vs No) as fixed effect.

c: In Study 064, treatment comparison was made using a n MMRM with baseline Hb as a covariate, and treatment, visit, visit-by-treatment interaction, ESA dependent incident dialysis within \leq 4 months vs > 4 months of starting dialysis when randomized, and randomization stratification factors except mean qualifying screening hemoglobin (\leq 10.5 vs > 10.5 g/dL) as fixed effects.

^d: In Study 002, the averages and difference in averages of the LSMeans from Weeks 28 to 36 with the corresponding CI were calculated from an MMRM with terms for the baseline Hb measurement as covariate and treatment group, visit and treatment by visit interaction, cardiovascular/cerebrovascular/thromboembolic history, geographical region (US versus Ex-US), and incident versus stable dialysis (\leq 4 versus > 4 months) as fixed effects. The unstructured covariance matrix was used to model the covariate structure.

e: Treatment comparison was made using an MMRM with baseline Hb as covariate and study, treatment, visit, visit-by-treatment interaction, study-by-treatment interaction, and history of cardiovascular/cerebrovascular/ thromboembolic diseases (Yes vs No) as fixed effects.

5.2.3.2.2. Hb Response with Roxadustat Compared to ESA in Patients with Inflammation at Baseline

Roxadustat demonstrated non-inferiority compared to ESA in increasing Hb levels in patients with DD CKD with evidence of inflammation at baseline (hsCRP > ULN) (Table 30). The analysis based on quintiles of hsCRP at baseline is presented in the Executive Summary of this document (Figure 18).

Table 30: DD Studies: Mean Change in Hb From Baseline to Mean Over Weeks 18 to 24 Regardless of Rescue Therapy in Patients with Baseline hsCRP > ULN

	Stud	y 063	Stud	y 064		y 002 CT)	DD	Pool
	Roxa	EPO	Roxa	EPO	Roxa	EPO	Roxa	EPO
Hb (g/dL)	n=228	n=222	n=189	n=176	n=306	n=319	n=720	n=714
Baseline								
n	228	222	189	176	280	301	720	714
M (CD)	8.54	8.38	10.30	10.24	10.05	0.06	9.62	9.52
Mean (SD)	(0.968)	(0.961)	(0.616)	(0.630)	10.05	9.96	(1.221)	(1.301)
Median	8.73	8.43	10.28	10.25	NA	NA	9.79	9.71
Min, Max	5.8, 10.1	5.6, 10.3	8.8, 11.8	8.6, 12.0	NA	NA	5.8, 11.9	5.6, 12.1
Average Hb in Wee	eks 18–24 (C	bserved + I	mputed)					
n	228	222	189	176	NA	NA	720	714
Mann (CD)	10.87	10.85	10.91	10.21	NIA	NIA	10.90	10.61
Mean (SD)	(1.043)	(1.023)	(0.927)	(0.755)	NA	NA	(0.981)	(1.030)
Median	10.99	10.97	11.06	10.22	NA	NA	11.02	10.63
Min, Max	7.5, 13.1	7.6, 13.8	7.8, 12.8	8.2, 12.5	NA	NA	7.5, 13.3	7.2, 14.8
ANCOVA with Mu	ıltiple Impu	tations						
LCM (CE)	2.29	2.27	0.55	-0.14	0.80	0.59	1.32	1.03
LSMean (SE)	(0.073)	(0.076)	(0.110)	(0.108)	(0.077)	(0.076)	(0.039)	(0.039)
050/ CI	(2.150,	(2.123,	(0.332,	(-0.350,	(0.64,	(0.44,	(1.244,	(0.954,
95% CI	2.438)	2.420)	0.764)	0.074)	0.95)	0.74)	1.398)	1.105)
LSMean Difference (SE)	0.02 (0.02 (0.099)		0.69 (0.093)		0.20 (0.081)		0.055)
95% CI	(-0.171	, 0.217)	(0.503,	0.869)	(0.04,	0.36)	(0.184,	0.400)

Abbreviations: ANCOVA=analysis of covariance; CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; Hb=hemoglobin; ITT=intent-to-treat analysis set; LSMean=least squares mean; Max=maximum; Min=minimum; Roxa=Roxadustat; SD=standard deviation; SE=standard error.

Note: Full analysis set.

5.2.3.2.3. Average Monthly IV Iron Use Over Weeks 28 to 52

Roxadustat patients required less monthly IV iron than EPO patients (52.2 mg vs 66.8 mg, respectively) to achieve the presented Hb response (Table 31).

Table 31: DD Studies: Average Monthly IV Iron Use^a Per Patient Exposure Month Over Weeks 28 to 52

IV Iron	Study 063		Stud	Study 064		Study 002 (ITT)		DD Pool	
(mg)	Roxa n=522	EPO n=513	Roxa n=369	EPO n=370	Roxa n=1051	EPO n=1055	Roxa n=1929	EPO n=1928	
n	437	438	286	319	885	920	1656	1716	
Mean (SD)	59.08 (145.179)	63.99 (98.771)	17.07 (53.375)	37.02 (106.778)	58.71 (236.12)	91.37 (225.64)	52.16 (226.293)	66.82 (162.076)	
Min, Max	0.0, 1600.0	0.0, 717.7	0.0, 515.8	0.0, 1400.0	0.0, 5600.0	0.0, 2800.0	0.0, 5504.0*	0.0, 2800.0	
p-Value	0.00	028 ^b	0.000	0.00091 °		< 0.0001 d		< 0.0001 d	

Abbreviations: ANCOVA=analysis of covariance; DD=dialysis-dependent; EOS=end of study; EPO=epoetin alfa; FAS=full analysis set; ITT=intent-to-treat analysis set; IV=intravenous; Max=maximum; Min=minimum; Roxa=roxadustat; SD=standard deviation.

Note: Full analysis set.

5.2.3.2.4. Mean LDL Cholesterol Changes from Baseline to Mean Over Weeks 12 to 28

Treatment with roxadustat compared with the EPO was associated with a decrease in LDL cholesterol from baseline to the average over Weeks 12 to 28 (-17.2 mg/dL versus -1.4 mg/dL) (Table 32).

^a: Monthly iron use for each patient=Total IV iron in mg/ ([last visit date - first dose date of study medication in the period+1]/28).

b: p-value is based on Koch et al (1982, 1990) stratified rank ANCOVA analysis, which was stratified by iron repletion status and randomization stratification factors except mean qualifying screening hemoglobin (≤ 8.0 g/dL versus

status and randomization stratification factors except mean qualifying screening nemoglobin (\leq 8.0 g/dL) and considering baseline hemoglobin as covariates for the comparison between roxadustat and epoetin alfa.

c: p-value is based on Koch et al. (1982, 1990) stratified rank ANCOVA analysis, which was stratified by iron repletion status and randomization stratification factors except mean qualifying screening hemoglobin ($\leq 10.5 \text{ vs} > 10.5 \text{ g/dL}$) and considering baseline Hb as covariates for the comparison between roxadustat and epoetin alfa.

d: p-value is from Wilcoxon Rank-Sum Test.

^{#:} În Study 002, IV iron data were collected from Week 36 to EOS in the ITT Population.

^{*:.} The max in the pooled analysis was calculated as the weighted average IV iron use during Weeks 28–36 and Weeks 37–52.

Table 32: DD Studies: Mean Change in LDL Cholesterol from Baseline to Mean Over Weeks 12 to 28

LDL	Stud	y 063	Stud	y 064	Stud	y 002	DD	Pool
LDL (mg/dL)	Roxa	EPO	Roxa	EPO	Roxa	EPO	Roxa	EPO
(mg/uL)	n=522	n=513	n=369	n=370	n=1051	n=1055	n=1929	n=1928
Baseline LDL ^a								
n	522	513	369	370	991	1002	1870	1875
Mean (SD)	109.12	109.22	84.53	84.45	87.70	87.78	93.25	93.02
Mean (SD)	(38.833)	(35.914)	(34.009)	(34.124)	(39.91)	(40.63)	(39.778)	(39.359)
Median	105.00	107.50	80.0	81.0	82.00	81.99	88.00	89.00
Min May	33.0,	26.0,	0.0.224.0	14.0,	13.0,	11.0,	0.0.261.0	11.0,
Min, Max	271.0	229.5	9.0, 234.0	186.0	361.9	314.0	9.0, 361.9	314.0
Average LDL in W	eeks 12–28							
n	487	481	327	354	950	982	1650	1741
M (CD)	85.84	104.33	71.19	85.65	74.51	87.00	76.67	91.81
Mean (SD)	(34.081)	(36.377)	(28.444)	(33.768)	(34.19)	(39.97)	(32.953)	(38.540)
Median	83.50	102.00	68.00	82.33	69.41	81.10	72.32	87.39
M: M	14.5,	10.0,	14.0,	17.0,	5.0.226.2	(0.269.0	7.2.259.0	7.0.269.0
Min, Max	258.0	252.0	195.7	252.0	5.0, 226.2	6.0, 268.0	7.3, 258.0	7.0, 268.0
ANCOVA								
LOM (CE)	-25.76	-7.42	-12.23	2.44	-14.54	-1.76	-17.22	-1.42
LSMean (SE)	(1.220)	(1.228)	(1.485)	(1.459)	(1.00)	(1.00)	(0.634)	(0.619)
95% CI	(-28.152,	(-9.828,	(-15.140,	(-0.421,	(-16.63,	(-3.87,	(-18.460,	(-2.631, -
95% CI	-23.362)	-5.007)	-9.310)	5.306)	12.37)	0.39)	-15.974)	0.205)
LSMean								
Difference (R -	-18.34 (1.584) ^c	-14.67	(1.514)	-12.76	(1.16)	-15.80	(0.885)
Comparator)								
95% CI	(-21.448,	-15.232)	(-17.640,	-11.695)	(-15.08,	-10.49)	(-17.535, -14.063)	
p-value	< 0.0	0001	< 0.0	0001	< 0.	001	< 0.0	0001

Abbreviations: ANCOVA=analysis of covariance; CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; LDL=low-density lipoprotein; LSMean=least squares mean; Max=maximum; Min=minimum; Roxa=roxadustat; SD=standard deviation; SE=standard error.

Note: Full analysis set.

5.2.3.2.5. Proportion of Patients Who Received RBC Transfusions During Treatment

As shown in Table 33, 9.5% of patients in the roxadustat group required RBC transfusion compared to 12.8% in the EPO group.

^a: Baseline is defined as the last available value prior to the first dose of study treatment.

Table 33: DD Studies: Proportion of Patients with RBC Transfusion in Roxadustat-Treated and Epoetin Alfa-Treated Patients with DD CKD

RBC	Stud	Study 063		y 064	Study 00	2 (ITT)	DD I	Pool
Transfusion	Roxa n=522	EPO n=513	Roxa n=369	EPO n=370	Roxa n=1048	EPO n=1053	Roxa n=1929	EPO n=1928
Patients with events a n (%)	38 (7.3)	33 (6.4)	46 (12.5)	78 (21.1)	103 (9.8)	139 (13.2)	184 (9.5)	246 (12.8)
Patients censored ^b n (%)	484 (92.7)	480 (93.6)	323 (87.5)	292 (78.9)	NA	NA	1745 (90.5)	1682 (87.2)
Treatment Effect (Roxa-ESA) HR ^c	1.26		0.67		0.83		0.82	
95% CI °	(0.791, 2.016)		(0.466, 0.970)		(0.64, 1.07)		(0.679, 0.997)	
p-value ^c	0.32	284	0.03	337	0.151		0.0461	

Abbreviations: CI=confidence interval; CKD=chronic kidney disease; DD=dialysis-dependent; EPO=epoetin alfa; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; HR=hazard ratio; ITT=intent-to-treat analysis set; NE=not estimable; NA=not available; PEY=patient exposure year; RBC=red blood cell; Roxa=roxadustat.

Note: Full analysis set.

5.2.3.2.6. Primary Efficacy Endpoint Results in Patients with ID-DD CKD

The mean change from baseline in Hb averaged over Weeks 28 to 52 regardless of rescue therapy was non-inferior in the roxadustat group compared to the EPO group (Table 34).

^a Any use of RBC transfusion.

^b Patients with no event were censored at the date of minimum (last dose date, last visit date, death date).

^c From a stratified Cox Proportional hazards model adjusting for treatment stratified by study, baseline Hb ($< 10 \text{ g/dL vs} \ge 10 \text{ g/dL}$) and history of cardiovascular/cerebrovascular/thromboembolic diseases (Yes vs No).

Note: In Study 002, patients who did not experience RBC transfusions were censored at the earliest occurrence of either 3 days after their last intake of study drug, or the date of withdrawal of consent or last study contact if the patient withdrew consent or was lost to follow-up, or at the date of death.

Table 34: ID-DD Subpopulation: Mean Change in Hb From Baseline to Mean Over Weeks 28 to 52 Regardless of Rescue Therapy

	Study 063		Study (ID St		Study (ID St	•	ID 1	Pool
	Roxa	EPO	Roxa	EPO	Roxa	EPO	Roxa	EPO
Hb (g/dL)	n=522	n=521	n=36	n=35	n=202	n=214	n=760	n=770
Baseline Hb								
N	522	521	36	35	202	214	760	770
Mana (CD)	8.43	8.46	10.23	10.09	9.56	9.62	8.82	8.86
Mean (SD)	(1.044)	(0.964)	(0.795)	(0.913)	(1.158)	(1.238)	(1.215)	(1.194)
Median	8.60	8.60	10.27	10.23	9.60	9.72	8.88	8.87
Min, Max	5.3, 10.2	5.0, 10.3	8.4, 11.8	8.6, 11.9	6.4, 12.0	6.0, 12.0	5.3, 12.0	5.0, 12.0
Average Hb in We	eks 28 to 52	(Observed +	Imputed)					
n	522	521	36	35	202	214	760	770
Maan (CD)	11.00	10.83	10.60	10.20	10.82	10.74	10.94	10.77
Mean (SD)	(0.819)	(0.876)	(0.785)	(0.782)	(0.896)	(1.010)	(0.842)	(0.919)
Median	11.09	10.89	10.63	10.23	10.92	10.77	11.03	10.82
Min, Max	8.0, 13.5	6.8, 13.2	8.9, 12.2	8.0, 11.9	7.8, 13.0	8.0, 13.3	7.7, 13.5	6.8, 13.3
ANCOVA with Mu	ıltiple Impu	tations						
I CMoon (CE)	2.38	2.20	0.51	0.07	1.23	1.15	1.90	1.67
LSMean (SE)	(0.041)	(0.041)	(0.164)	(0.155)	(0.078)	(0.073)	(0.063)	(0.065)
95% CI	(2.298,	(2.115,	(0.185,	(-0.239,	(1.083,	(1.008,	(1.772,	(1.546,
93% CI	2.461)	2.278)	0.829)	0.369)	1.387)	1.294)	2.020)	1.801)
LSMean Difference (SE)	0.18 ((0.053)	0.44 (0.225)	0.08 (0.103)	0.22 (0.090)
95% CI	(0.079)	, 0.287)	(0.001,	, 0.883)	(-0.118	, 0.286)	(0.047)	, 0.399)

Abbreviations: ANCOVA=analysis of covariance; CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; Hb=hemoglobin; ID=incident dialysis; LSMean=least squares mean; Max=maximum; Min=minimum;

Roxa=roxadustat; SD=standard deviation; SE=standard error.

Note: Intent-to-treat analysis set.

6. CLINICAL SAFETY

6.1. Overview of Safety Evaluation Plan

The pooled safety analysis population consisted of all randomized patients who received at least one dose of study drug in 3 pooled NDD studies (Studies 001, 060, and 608), and 3 pooled DD studies (002, 063, and 064), consisting of 4,326 patients treated with roxadustat, 1,884 patients treated with placebo and 1940 patients treated with EPO. CV safety was examined using events that were adjudicated by an independent committee blinded to treatment assignment.

In addition, supportive data from Study 610 (consisting of 323 patients treated with roxadustat and 293 patients treated with EPO) are presented due to that study's unique design as an active-controlled NDD trial which was not affected by bias due to different study drug discontinuation. Data from Study 613 (Study 613, consisting of 414 patients treated with roxadustat, 257 patients treated with EPO, and 163 patients treated with darbepoetin alfa) were excluded from the pooled DD CKD analyses because this study included 2 comparators (EPO and darbepoetin alfa), different from other 3 DD studies with a single active comparator (EPO).

6.2. Safety Data/Endpoints (NDD and DD)

Safety data collection included AEs, SAEs, discontinuation of study medication due to AEs, and other standard safety measures (eg, laboratory values, vital signs, electrocardiogram, etc). All reported AEs for the pivotal studies were collected while patients remained on treatment up to 28 days, and those events occurring within this OT+28-day period were considered treatment-emergent. The approach to safety data collection following the OT+28-day period varied among the pivotal trials. In Study 608, patients that discontinued treatment prematurely were assessed every 6 months until the end of the study for vital status, SAEs, and CV and thromboembolic events, unless consent was withdrawn; Studies 063, 064, and 060 conducted telephone visits every 3–6 months to assess for CV events; and Studies 001 and 002 favored continued study visits with no change to safety data collection, but allowed for modified follow-up such as telephone visits, when necessary to avoid withdrawal of consent.

The key CV safety endpoints were as follows:

- MACE: consisting of adjudicated events of myocardial infarction, stroke, and ACM
- MACE +: MACE plus additional adjudicated events of hospitalized unstable angina and hospitalized congestive heart failure
- ACM: all-cause mortality

6.3. Clinical Safety–Overall Extent of Exposure (NDD and DD)

A total of 9,600 patients with CKD anemia were exposed to the study drugs (roxadustat, placebo, EPO) in the Phase 3 studies as shown in Table 35.

Table 35: Total Exposure to Study Drugs in Phase 3 Studies

		l Study 01	Pivotal S	study 060	Pivotal S	Study 608	NDD	Pool		ive Study 10
NDD	Roxa	Placebo	Roxa	Placebo	Roxa	Placebo	Roxa	Placebo	Roxa	Darbe- poetin Alfa
Patient Number	1384	1376	611	305	391	203	2386	1884	323	293
PEY a	2263.1	1747.6	1134.9	377.3	472.7	198.3	3870.7	2323.2	519.3	472.5
PY ^b	2943.8	2918.7	1307.8	541.1	546.0	261.6	4797.7	3721.4	540.6	504.2
		l Study 02	Pivotal S	study 063	Pivotal S	Study 064	DD	Pool		ive Study 13
DD	Roxa	Epoetin	Roxa	Epoetin	Roxa	Epoetin	Roxa	Epoetin	Roxa	ESAsc
Patient Number	1048	1053	522	517	370	370	1940	1940	414	420

Abbreviations: CKD=chronic kidney disease; DD=dialysis-dependent; ESA=erythropoiesis-stimulating agent;

6.4. Cardiovascular Safety

6.4.1. Cardiovascular Safety in NDD Population

Table 36 shows retention and follow-up in the pooled NDD studies.

Table 36: NDD Studies: Retention and Follow-up (% Based on Patients Who Were Randomized and Received at Least One Dose of Study Drug)

	0	01	0	060		608		Pooled NDD Studies	
	Roxa n (%) (N=1384)	Placebo n (%) (N=1376)	Roxa n (%) (N=611)	Placebo n (%) (N=305)	Roxa n (%) (N=391)	Placebo n (%) (N=203)	Roxa n (%) (N=2386)	Placebo n (%) (N=1884)	
Study completed on study drug	885 (63.9)	575 (41.8)	349 (57.1)	98 (32.1)	245 (62.7)	89 (43.8)	1479 (62.0)	762 (40.4)	
Study completed follow-up in MACE (full data on MACE)	1304 (94.2)	1254 (91.1)	479 (78.4)	206 (67.5)	316 (80.8)	145 (71.4)	2099 (88.0)	1605 (85.2)	
Study completed follow-up in Vital status (ascertained at end of study ie, alive or dead)	1374 (99.3)	1362 (99.0)	481 (78.7)	211 (69.2)	312 (79.8)	143 (70.4)	2167 (90.8)	1716 (91.1)	

Abbreviations: MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); NDD=non-dialysis-dependent; Roxa=roxadustat.

Table 37 shows the results for MACE, and of MACE+, and ACM with roxadustat compared to placebo.

NDD=non-dialysis-dependent; Roxa=roxadustat.

^a Patient exposure years (PEY) for each patient=(last dose date - first dose date + 1) / 365.25.

b Patient follow-up years (PY) for each patient=(date of last known vital status – first dose date + 1)/365.25.

^c Active controls were epoetin alfa and darbepoetin alfa in Study 613.

Safety Population, NDD Pool: Studies 001, 060,608; DD Pool: Studies 002, 063, 064

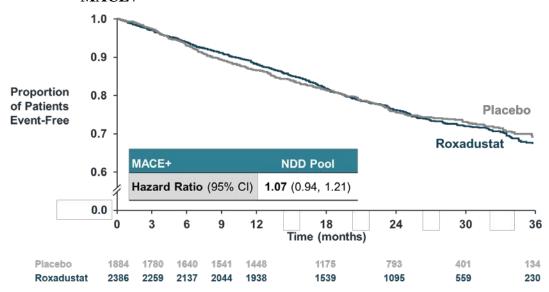
Table 37: Pooled NDD Studies: Primary Analysis of MACE, MACE+, and All-Cause Mortality

	MA	CE	MA	CE+	AC	CM
On-Study Analysis	Roxadustat	Placebo	Roxadustat	Placebo	Roxadustat	Placebo
NDD Set	(n=2386)	(n=1884)	(n=2386)	(n=1884)	(n=2386)	(n=1884)
Total PY	4509.6	3406.2	4368.9	3272.4	4797.7	3721.4
No. patients with events	480	350	578	432	400	301
IR/100 PY	10.6	10.3	13.2	13.2	8.3	8.1
HR (95% CI)	1.10 (0.9	96, 1.27)	1.07 (0.9	94, 1.21)	1.08 (0.9	93, 1.26)

Abbreviations: ACM=all-cause mortality; CI=confidence interval; HR=hazard ratio; IR=incidence rate; on-study analysis=analysis evaluation period to include on-treatment and off-treatment long-term follow-up, until end of study; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure; PY=patient follow-up years. Note: Safety Population; On-study analysis, NDD Pool: Studies 001, 060,608.

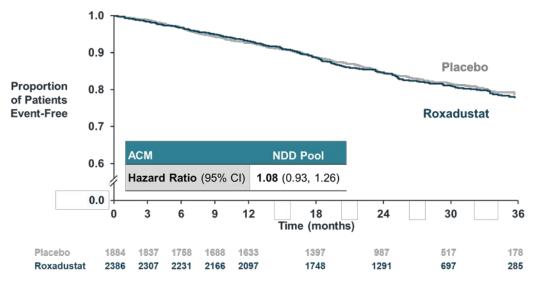
The Kaplan-Meier survival analysis plots for the endpoints of MACE show the probability of remaining event-free over time (Figure 39). Survival curves of the 2 treatment groups tracking closely together in all 3 endpoints are supportive of the comparable risks of MACE, MACE+ (Figure 61), and ACM (Figure 62) between roxadustat and placebo.

Figure 61: Pooled NDD Studies: Kaplan-Meier Curves of Primary Analysis of MACE+



Abbreviations: CI=confidence interval; MACE+=major adverse cardiovascular events (all-cause mortality, myocardial infarction, and stroke) plus hospitalization for unstable angina or congestive heart failure; NDD=non-dialysis-dependent. Note: Safety Population; On-study analysis, NDD Pool: Studies 001, 060,608, hazard ratio upper bound of 95% CI below reference margin of 1.3.

Figure 62: Pooled NDD Studies: Kaplan-Meier Curves of Primary Analysis of ACM

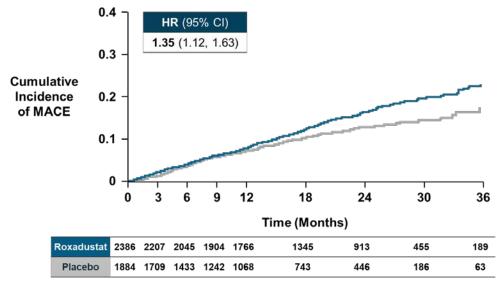


Abbreviations: ACM=all-cause mortality; CI=confidence interval; NDD=non-dialysis-dependent Note: Safety Population; On-study analysis, NDD Pool: Studies 001, 060,608, hazard ratio upper bound of 95% CI below reference margin of 1.3.

On-treatment Analysis of MACE in the NDD pool

Figure 63 shows the Kaplan-Meier curve for MACE in the NDD pool in the OT+28 days analysis set. The curves track closely together until 9–12 months following randomization and then separate due to decreasing event rates in the placebo group, consistent with observed differences in rates of MACE being due to informative censoring in the placebo group.

Figure 63: Pooled NDD Studies: MACE Results in the OT+28 Analysis Set



Abbreviations: CI=confidence interval; HR=hazard ratio; MACE=major adverse cardiovascular events (all-cause mortality, myocardial infarction, and stroke); OT+28=on-treatment plus 28 days.

Study 001 Cardiovascular Safety Results

Table 38: Study 001: Cardiovascular Safety Results

	Roxadustat	Placebo	
	N=1376	N=1384	
Overall population	n (%)	n (%)	HR (95% CI)
MACE	332 (24.1)	287 (20.1)	1.13 (0.96, 1.32)
MACE+	394 (28.6)	352 (25.4)	1.10 (0.95, 1.27)
ACM	284 (20.6)	245 (17.7)	1.15 (0.97, 1.37)
	Roxadustat	Placebo	
	N=1376	N=1384	
NDD-NDD	n (%)	n (%)	HR (95% CI)
MACE	211 (15.3)	206 (14.9)	1.04 (0.86, 1.26)
MACE+	273 (19.8)	258 (18.6)	1.07 (0.90, 1.27)
ACM	178 (12.9)	171 (12.4)	1.07 (0.87, 1.33)
	Roxadustat	Placebo	
	N=1093	N=1094	
NDD eGFR ≥ 10	n (%)	n (%)	HR (95% CI)
MACE	238 (21.8)	220 (20.1)	1.04 (0.87, 1.25)
MACE+	283 (25.9)	269 (24.6)	1.04 (0.88, 1.24)
ACM	201 (18.4)	187 (17.1)	1.05 (0.86, 1.28)

Abbreviations: ACM=all-cause mortality; CI=confidence interval; eGFR=estimated glomerular filtration rate; HR=hazard ratio; MACE=major adverse cardiovascular events (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure; NDD=non-dialysis-dependent. Note: Safety Population; On-study analysis.

6.4.1.1. Placebo Evaluation Period Adjusted Analysis

Due to the differential discontinuation rates between the roxadustat and placebo groups in the pooled NDD population that result in informative censoring which biases event rate comparison in on-treatment analyses, a more appropriate comparison is to disregard the treatment-emergent window and allow comparisons to be based on equal follow-up time. One method, the placebo evaluation period adjusted method, adjusts the follow-up time in patients on placebo who were censored at OT+28 to be comparable to the expected time at risk accrued through OT+28 in patients on roxadustat with the same baseline characteristics that were associated with the risk of major clinical events.

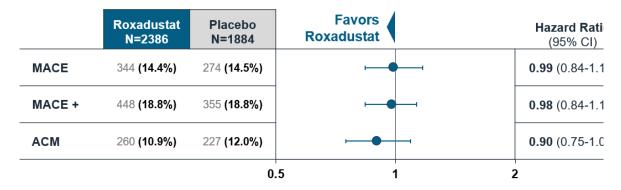
The observed OT+28 window of placebo patients is replaced by a randomly selected OT+28 window from a donor pool of roxadustat patients with similar baseline characteristics. This process is repeated 1000 times. The final estimate of HR and its 95% CI are obtained from the MI (MIANALYZE) procedure.

Note that only the event evaluation periods of the placebo patients are adjusted. Additional events that occurred in the placebo patients that were originally not included may now be

included in the analysis only because of the lengthening of the evaluation period. There is no imputation on the occurrence of the events.

Figure 64 shows results using the placebo evaluation period adjusted method for MACE, MACE+, and ACM. HR point estimates range from 0.90–0.99, with 95% CIs which cross 1.0 with upper bounds of 1.09–1.17.

Figure 64: Pooled NDD Studies: Forest Plot of Analyses of MACE, MACE+, and ACM Using the Placebo Evaluation Period Adjusted Method



Abbreviations: ACM=all-cause mortality; CI=confidence interval; eGFR=estimated glomerular filtration rate; HR=hazard ratio; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure; NDD=non-dialysis-dependent. Note: HR is estimated using the Cox regression model by study in each sampling replicate. The Cox model includes cardiovascular/cerebrovascular/thromboembolic medical history (yes vs no), geographical region (Europe vs ex-Europe), baseline hemoglobin ($< 8 \text{ g/dL vs} \ge 8 \text{ g/dL}$) and baseline eGFR ($< 10 \text{ mL/min/1.73 m}^2 \text{ vs} \ge 10 \text{ mL/min/1.73 m}^2$) as strata. The final HR and the 95% CI are estimated using MIANALYZE.

6.4.1.2. All-Cause Mortality in Pivotal Phase 3 NDD Studies: Cause of Death

The rates of all-cause deaths were comparable in the roxadustat group and the placebo group. Adjudicated causes of death are presented in Table 39.

Table 39: Pooled NDD Pooled: All-Cause Mortality

NDD ITT		dustat PY=4797.7)		cebo PY=3721.4)
	n (%)	IR/100 PY a	n (%)	IR/100 PY a
Total Number of Deaths	400 (16.8)	8.3	301 (16.0)	8.1
Cardiovascular-related	143 (6.0)	3.0	102 (5.4)	2.7
Sudden cardiac death	66 (2.8)	1.4	42 (2.2)	1.1
Stroke	21 (0.9)	0.4	14 (0.7)	0.4
Acute myocardial infarction	20 (0.8)	0.4	23 (1.2)	0.6
Heart failure	19 (0.8)	0.4	15 (0.8)	0.4
Other CV causes	9 (0.4)	0.2	3 (0.2)	0.1
CV procedure	7 (0.3)	0.1	1 (0.1)	0.0
CV hemorrhage	1 (0.0)	0.0	4 (0.2)	0.1
Non-cardiovascular-related	185 (7.8)	3.9	116 (6.2)	3.1
Infection	87 (3.6)	1.8	39 (2.1)	1.0
Renal	54 (2.3)	1.1	37 (2.0)	1.0
Malignancy	11 (0.5)	0.2	8 (0.4)	0.2
Pancreatic	5 (0.2)	0.1	4 (0.2)	0.1
Hemorrhage	5 (0.2)	0.1	10 (0.5)	0.3
Hepatobiliary	4 (0.2)	0.1	3 (0.2)	0.1
Trauma	4 (0.2)	0.1	3 (0.2)	0.1
Non-CV procedure	4 (0.2)	0.1	4 (0.2)	0.1
Gastrointestinal	3 (0.1)	0.1	4 (0.2)	0.1
Inflammatory Immune/ Autoimmune	3 (0.1)	0.1	0 (0.0)	0
Neurological	3 (0.1)	0.1	2 (0.1)	0.1
Pulmonary	2 (0.1)	0	1 (0.1)	0
Suicide	0 (0.0)	0	1 (0.1)	0
Undetermined	72 (3.0)	1.5	83 (4.4)	2.2

Abbreviations: CV=cardiovascular; IR=incidence ratio; ITT=intent-to-treat analysis set; NDD=non-dialysis-dependent; PY=patient year.

6.4.2. Cardiovascular Safety in DD Population

Table 40 shows retention and follow-up in the pooled NDD studies.

 $^{^{}a}$ IR/100 PY=100 x number of patients with events / PY. PY for each patient=(first event occurrence or censor date - first dose date + 1) / 365.25.

Safety Population; On-Study evaluation period, NDD Pool: Studies 001, 060, 608.

Table 40: DD Studies: Retention and Follow-up (% Based on Patients Who Were Randomized and Received at Least One Dose of Study Drug)

	Stud	Study 002		y 063	Stud	y 064	Pooled DD Studies	
	Roxa	EPO	Roxa EPO		Roxa EPO		Roxa	EPO
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	(N=1048)	(N=1053)	(N=522)	(N=517)	(N=370)	(N=370)	(N=1940)	(N=1940)
Study completed on study drug	696 (66.4)	796 (75.6)	307 (58.8)	308 (59.6)	127 (34.3)	183 (49.5)	1130 (58.2)	1287 (66.3)
Study completed follow-up in MACE (full data on MACE)	989 (94.4)	993 (94.3)	442 (84.7)	431 (83.4)	288 (77.8)	315 (85.1)	1719 (88.6)	1739 (89.6)
Study completed follow-up in Vital status (ascertained at end of study ie, alive or dead)	1043 (99.5)	1047 (99.4)	437 (83.7)	428 (82.8)	282 (76.2)	310 (83.8)	1762 (90.8)	1785 (92.0)

Abbreviations: DD=dialysis-dependent; EPO=epoetin alfa; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); Roxa=roxadustat.

Table 41 shows the results of analyses of MACE, MACE+, and ACM with roxadustat treatment compared to placebo.

Table 41: Pooled DD Studies: Primary Analysis of MACE, MACE+, and All-Cause Mortality

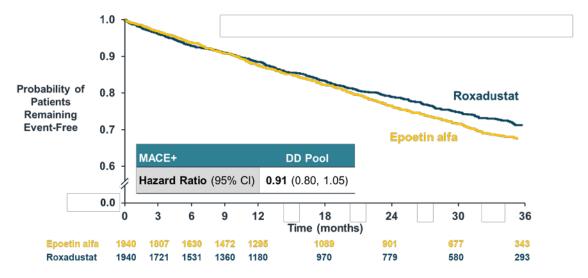
DD	MA	CE	MA	CE+	ACM		
OT+7	Roxadustat	EPO	Roxadustat	Roxadustat EPO		EPO	
	(n=1940)	(n=1940)	(n=1940)	(n=1940)	(n=1940)	(n=1940)	
Total PY	3315.3	3743.6	3315.3	3743.6	3315.3	3743.6	
No. of patients with events	306	339	373	458	207	232	
IR/100 PY	9.2	9.1	11.3	12.2	6.2	6.2	
HR (95% CI)	1.02 (0.8	1.02 (0.88, 1.20)		30, 1.05)	1.02 (0.84, 1.23)		

Abbreviations: ACM=all-cause mortality; CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; IR=incidence rate; HR=hazard ratio; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalization for unstable angina or congestive heart failure; OT+7=on-treatment plus 7 days; PY=patient years.

Note: Safety Population, OT+7 analyses, DD Pool: Studies 002, 063, 064

The Kaplan-Meier survival analysis plots for the endpoints of MACE show the probability of remaining event-free over time (Figure 44). Survival curves of the 2 treatment groups tracking closely together in all 3 endpoints are supportive of the comparable risks of MACE, MACE+ (Figure 65) and ACM (Figure 66) between roxadustat and placebo.

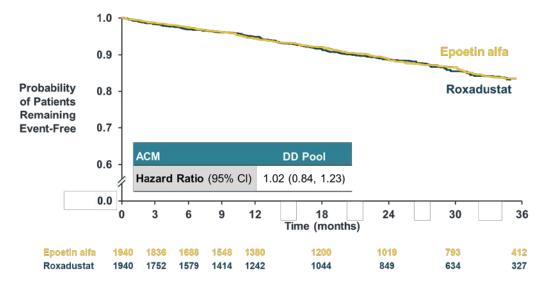
Figure 65: Pooled DD Studies: Kaplan-Meier Survival Curves of MACE+



Abbreviations: CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; FAIR=Follow-up adjusted incidence rate; MACE+=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke) plus hospitalizations for unstable angina or congestive heart failure; OT+7=on-treatment plus 7 days.

Note: Safety Population, OT+7 analyses, DD Pool: Studies 002, 063, 064

Figure 66: Pooled DD Studies: Kaplan-Meier Curves of Primary Analysis of ACM



Abbreviations: ACM=all-cause mortality; CI=confidence interval; DD=dialysis-dependent; OT+7=on-treatment plus 7 days.

Note: Safety Population, OT+7 analyses, DD Pool: Studies 002, 063, 064.

In agreement with FDA, on-treatment plus 7 days (OT+7) was chosen as the primary analysis set for CV safety in the DD population. This analysis was chosen to allow for the capture of residual safety events, while minimizing confounding due to Hb fluctuation and/or ESA treatment following roxadustat discontinuation. OT+28 was agreed to as a supportive analysis, and the HR (95% CI) for MACE was 1.08 (0.94, 1.25) (Figure 67).

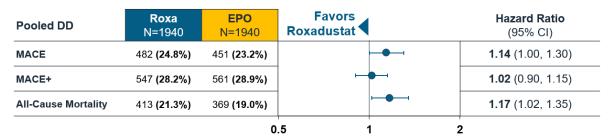
Figure 67: Pooled DD Studies: Forest Plot of MACE, MACE+, and ACM (OT+28)

DD Pool	Roxadustat N = 1940	Epoetin Alfa N = 1940	Favors Roxadustat	Hazard Ratio (95% CI)
MACE	370 (19.1%)	388 (20.0%)	—	1.08 (0.94, 1.25)
MACE+	437 (22.5%)	504 (26.0%)	<u> </u>	0.97 (0.85, 1.10)
ACM	282 (14.5%)	293 (15.1%)	-	1.09 (0.93, 1.29)
		0	.5 1	2

Abbreviations: ACM=all-cause mortality; CI=confidence interval; DD=dialysis-dependent; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalizations for unstable angina or congestive heart failure; OT+28=on-treatment plus 28 days. Roxa=roxadustat. Note: Safety Population, OT+28 Analysis, DD Pool: Studies 002, 063, 064.

On-study results for the DD population are presented below (Figure 68). One concern with the use of on-study analyses in this patient population is that these analyses will reflect the period of Hb adjustment when roxadustat patients who discontinued study treatment had to be titrated to standard of care ESA treatment, or alternatively a period of no anemia treatment which would be expected to lead to a reduction in Hb. No such titration period was required for EPO-treated patients who discontinued study treatment as they would be expected to continue on ESA (Figure 70). Consequently, the ITT analysis of the DD population is biased away from the null and against roxadustat compared to ESA. Notably, on-study results in the ID subgroup revealed HR point estimates of 0.87–1.01 (Figure 69).

Figure 68: Pooled DD Studies: Forest Plot of MACE, MACE+, and ACM (On-Study)



Abbreviations: ACM=all-cause mortality; CI=confidence interval; DD=dialysis-dependent; EPO=epoetin alfa; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalizations for unstable angina or congestive heart failure; Roxa=roxadustat. Note: Safety Population, On-Study Analysis, DD Pool: Studies 002, 063, 064.

Figure 69: Pooled ID Studies: Forest Plot of MACE, MACE+, and ACM (On-Study Analysis)

Pooled ID	Roxa N=760	EPO N=766	Favors Roxadustat	Hazard Ratio (95% CI)
MACE	111 (14.6%)	122 (15.9%)	<u> </u>	0.95 (0.73, 1.23)
MACE+	125 (16.4%)	147 (19.2%)		0.87 (0.68, 1.11)
All-Cause Mortality	97 (12.8%)	100 (13.1%)		1.01 (0.76, 1.35)
		0	.5 1	2

Abbreviations: ACM=all-cause mortality; CI=confidence interval; ID=incidence dialysis; EPO=epoetin alfa; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalizations for unstable angina or congestive heart failure; Roxa=roxadustat.

Note: Safety Population, On-study Analysis.

Figure 70: ESA Treatment Before, During, and After Treatment Discontinuation in the Roxadustat DD Program

ESA conversion		Study Drug	Post-Treatment		
	Pre-study Period	On Treatment (OT) Period	28 days	> 28 days to EoS	
	ESA-pretreated	Roxadustat		ESA	
		ESA		ESA	

	Study Drug		Post-Treatment		
Hb correction	Pre-study Period	On Treatment (OT) Period	28 days	> 28 days to EoS	
	ESA-untreated	Roxadustat		ESA	
		ESA		ESA	

Abbreviations: DD=dialysis-dependent; EOS=end of study; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin.

6.4.2.1. All-Cause Mortality in Pivotal Phase 3 DD Studies: Cause of Death

The rates of all-cause deaths were comparable in the roxadustat group and the placebo group. Adjudicated causes of death are presented in Table 42.

Table 42: Pooled DD Studies: All-Cause Mortality

	Rox	kadustat	Epoetin Alfa (N=1940, PEY=3743.6)		
DD	(N=1940,	PEY=3315.3)			
OT+7	n (%)	Incidence/100 PY	n (%)	Incidence/100 PY	
Total Number of Deaths	207 (10.7)	6.2	232 (12.0)	6.2	
Cardiovascular-related	122 (6.3)	3.7	136 (7.0)	3.6	
Sudden cardiac death	69 (3.6)	2.1	78 (4.0)	2.1	
Acute myocardial infarction	20 (1.0)	0.6	11 (0.6)	0.3	
Heart failure	16 (0.8)	0.5	14 (0.7)	0.4	
Stroke	7 (0.4)	0.2	19 (1.0)	0.5	
Other CV causes	5 (0.3)	0.2	6 (0.3)	0.2	
CV procedure	4 (0.2)	0.1	4 (0.2)	0.1	
CV hemorrhage	1 (0.1)	0.0	4 (0.2)	0.1	
Non-cardiovascular-related	67 (3.5)	2.0	72 (3.7)	1.9	
Infection	32 (1.6)	1	32 (1.6)	0.9	
Renal	9 (0.5)	0.3	5 (0.3)	0.1	
Gastrointestinal	4 (0.2)	0.1	7 (0.4)	0.2	
Hemorrhage	4 (0.2)	0.1	4 (0.2)	0.1	
Malignancy	4 (0.2)	0.1	6 (0.3)	0.2	
Trauma	3 (0.2)	0.1	3 (0.2)	0.1	
Hepatobiliary	2 (0.1)	0.1	1 (0.1)	0	
Pancreatic	2 (0.1)	0.1	2 (0.1)	0.1	
Neurological	2 (0.1)	0.1	1 (0.1)	0	
Non-CV procedure	2 (0.1)	0.1	6 (0.3)	0.2	
Inflammatory Immune/Autoimmune	1 (0.1)	0	2 (0.1)	0.1	
Other	1 (0.1)	0	1 (0.1)	0	
Pulmonary	1 (0.1)	0	0 (0.0)	0	
Suicide	0 (0.0)	0	1 (0.1)	0	
Drug reaction or overdose	0 (0.0)	0	1 (0.1)	0	
Undetermined	18 (0.9)	0.5	24 (1.2)	0.6	

Abbreviations: DD=dialysis-dependent; PEY=patient exposure year; OT+7=on-treatment plus 7 days.

Note: Safety Population, OT+7 analyses, DD pool: Studies 002, 063, 064.

6.5. General Safety Assessment of Roxadustat in NDD Population

6.5.1. Exposure in Pivotal NDD Studies

The large safety population of the NDD pool (n=4,270) from 3 pivotal Phase 3 studies includes 2,386 patients treated with roxadustat and 1,884 patients on placebo. No patients were on dialysis at the time of randomization, but ~ 35% of patients were initiated on dialysis during the study period. As shown in Table 43, mean duration of exposure and PY were greater in the roxadustat treatment group than in the placebo group due to the earlier and greater rates of study drug discontinuations in the placebo group resulting in a more pronounced difference in overall exposure to study treatment between the treatment groups.

Patient disposition and baseline demographics and other characteristics, including CV history, were generally similar for the treatment groups in the NDD pool.

Table 43: Pooled NDD Studies: Overall Drug Exposure (Safety Population)

	Roxadustat (N=2386)	Placebo (N=1884)
Patient Exposure (Week):		
Mean (SD)	84.6 (48.79)	64.3 (44.82)
Median (Min-Max)	87.1 (0 –234.9)	57.1 (0 –208.1)
Mean Exposure (Year)	1.6	1.2
Total PY	3870.7	2323.2

Abbreviations: NDD=non-dialysis-dependent; PY=patient year; SD=standard deviation.

Note: Safety Population, NDD Pool: Studies 001, 060, 608.

6.5.2. Safety Data from Pivotal NDD Studies

To account for differences in study drug exposure per treatment group in the NDD population, exposure-adjusted incidence rates are presented in addition to incidence. However, this does not account for overrepresentation of higher-risk patients in the roxadustat group for on-treatment analyses.

An overview of AEs in the pooled NDD studies is provided in Table 44. Most patients experienced at least 1 AE in both groups. Roxadustat-treated patients had slightly higher incidence rates of SAEs. Roxadustat-treated patients had higher incidence rate of fatal events during the treatment emergent period; however, ACM, which includes deaths both on treatment as well as during long-term follow-up period, was similar for both groups: 8.3 deaths per 100 PY for roxadustat and 8.1 deaths per 100 PY for placebo.

The incidence rate for AEs that led to discontinuation was similar for roxadustat and placebo (3.9 vs 3.8 per 100 PY).

Table 44: Pooled NDD Studies: Summary of Overall Treatment-Emergent Adverse Events in Roxadustat and Placebo Groups

		dustat 2386	Placebo N=1884		
	n (%)	IR/100 PY	n (%)	IR/100 PY	
Any AEs	2132 (89.4)	222.6	1608 (85.4)	211.5	
Any SAEs	1308 (54.8)	45.9	845 (44.9)	43.9	
AEs leading to discontinuation	157 (6.6)	3.9	92 (4.9)	3.8	
Any Fatal AEs	276 (11.6)	6.9	134 (7.1)	5.5	
All-Cause Mortality ^a	400 (16.8)	8.3	301 (16.0)	8.1	

Abbreviations: AE=adverse event; IR=incidence rate; ITT=intent=to=treat; N=number of patients within treatment group; n=number of patients with the specified event; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PY=patient year; SAE=serious adverse event.

^a All-cause deaths occurred during both on-treatment and long-term follow-up period (ITT analysis). Each death was adjudicated by a central adjudication committee that was blinded to treatment assignment. Note: Safety Population, OT+28 analyses, NDD pool: Studies 001, 060, 608.

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6.5.2.1. Common Treatment-Emergent Adverse Events

Treatment-emergent AEs reported in \geq 5% of patients in either group are presented in Table 45. The most commonly reported AEs in both roxadustat and placebo-treated patients were ESRD, hypertension, and peripheral edema. Other common events were mostly gastrointestinal events (ie, diarrhea, nausea, constipation, and vomiting), infections (urinary tract infection, upper respiratory infections, and pneumonia) and laboratory abnormalities (hyperkalemia and hypoglycemia). AEs with an incidence rate of > 1.0 patients per 100 PY in roxadustat versus placebo patients included hypertension, peripheral edema, hyperkalemia, diarrhea, urinary tract infection, nausea, constipation, and insomnia.

Table 45: Pooled NDD Studies: Summary of Treatment-Emergent Adverse Events (Incidence ≥ 5%) by Preferred Terms in Roxadustat and Placebo Groups

Preferred Term		Roxadustat N=2386		Placebo N=1884	
	n (%)	IR/100 PY	n (%)	IR/100 PY	
Any AE	2132 (89.4)	222.6	1608 (85.4)	211.5	
End-stage renal disease	437 (19.8)	13.0	282 (15.0)	12.1	
Hypertension	329 (13.8)	9.0	153 (8.1)	6.6	
Oedema peripheral	279 (11.7)	7.6	143 (7.6)	6.1	
Hyperkalemia	261 (10.9)	7.0	133 (7.1)	5.7	
Diarrhea	248 (10.4)	6.6	129 (6.8)	5.5	
Urinary tract infection	248 (10.4)	6.6	120 (6.4)	5.1	
Nausea	243 (10.2)	6.5	119 (6.3)	5.1	
Viral upper respiratory tract infection	228 (9.6)	6.2	137 (7.3)	6.0	
Pneumonia	212 (8.9)	5.5	118 (6.3)	4.9	
Constipation	209 (8.8)	5.5	102 (5.4)	4.3	
Upper respiratory tract infection	187 (7.8)	5.0	110 (5.8)	4.7	
Headache	178 (7.5)	4.7	103 (5.5)	4.4	
Cough	170 (7.1)	4.5	90 (4.8)	3.8	
Vomiting	148 (6.2)	3.8	76 (4.0)	3.2	
Dizziness	146 (6.1)	3.8	110 (5.8)	4.7	
Hypoglycemia	146 (6.1)	3.8	77 (4.1)	3.2	
Back pain	138 (5.8)	3.6	71 (3.8)	3.0	
Pruritus	138 (5.8)	3.6	86 (4.6)	3.6	
Insomnia	131 (5.5)	3.4	44 (2.3)	1.8	
Dyspnea	124 (5.2)	3.2	90 (4.8)	3.8	
Arthralgia	121 (5.1)	3.1	73 (3.9)	3.1	
Acute kidney injury	121 (5.1)	3.1	53 (2.8)	2.2	
Anemia	51 (2.1)	1.3	101 (5.4)	4.2	

Abbreviations: AE=adverse event; IR=incidence rate; N=number of patients within treatment group; n=number of patients with the specified event; NDD=non-dialysis-dependent; OT+28=on-treatment plus 28 days; PY=patient year. Note: $AEs \ge 5\%$ in either group, Safety Population, OT+28 analyses, NDD Pool: Studies 001, 060, 608.

6.5.2.2. Treatment-Emergent Adverse Events Leading to Discontinuation

The summary of AEs that led to treatment discontinuation is presented in Table 46. The overall incidence of AEs leading to discontinuation was comparable and low in both treatment groups. No single event leading to study discontinuation in any treatment group was reported in > 1% of patients.

Table 46: Pooled NDD Studies: Summary of Treatment-Emergent Adverse Events (≥ 0.3%) Leading to Discontinuation by Preferred Terms in Roxadustat and Placebo Groups

		dustat 2386	Placebo N=1884		
Preferred Term	n (%)	IR/100 PY	n (%)	IR/100 PY	
AEs leading to discontinuation	157 (6.6)	3.9	92 (4.9)	3.8	
End-stage renal disease	18 (0.8)	0.4	7 (0.4)	0.3	
Acute kidney injury	11 (0.5)	0.3	1 (0.1)	0.0	
Sepsis	6 (0.3)	0.1	1 (0.1)	0.0	
Anemia	2 (0.1)	0	8 (0.4)	0.3	
Fatigue	0	0	5 (0.3)	0.2	

Abbreviations: AE=adverse event; IR=incidence rate; N=number of patients within treatment group; n=number of patients with the specified event; NDD=non-dialysis-dependent; PY=patient year.

Note: AEs leading to discontinuation $\geq 0.3\%$ in either group, Safety Population, OT+28 analyses, NDD Pool: Studies 001, 060, 608.

6.6. General Safety Assessment of Roxadustat in DD Population

6.6.1. Exposure in Pivotal DD Studies

The pooled pivotal Phase 3 studies in patients with DD CKD include 1940 roxadustat-treated patients and 1940 EPO-treated patients. The exposure to treatment was shorter for the roxadustat group compared to EPO- (Table 47). The ID-DD subpopulation included 760 roxadustat-treated patients and 766 EPO-treated patients.

Table 47: Pooled DD Studies (ID-DD and SDD-DD Subpopulations): Overall Drug Exposure

	Poole	d DD Pool		ed ID	Pooled SDD	
	Roxadustat (N=1940)	Epoetin Alfa (N=1940)	Roxadustat (N=760)	Epoetin Alfa (N=766)	Roxadustat (N=1180)	Epoetin Alfa (N=1174)
Patient Exposure (Week):						
Mean (SD)	89.2 (58.69)	100.7 (57.54)	75.4 (57.62)	81.0 (60.29)	98.0 (57.68)	113.5 (51.82)
Median (Min-Max)	87.9 (0.1–227.9)	107.5 (0.1–226.9)	54.6 (0.4–227.9)	59.9 (0.1–226.9)	106.9 (0.1–195.7)	135.6 (0.4–195.4)
Mean Exposure (Year)	1.7	1.9	1.4	1.6	1.9	2.2

Abbreviations: DD=dialysis-dependent; ID=incident dialysis; Min=minimum; Max=maximum; SDD=stable dialysis-dependent; SD=standard deviation.

Note: Safety Population, DD Pool: Studies 002, 063, 064.

6.6.2. Safety Data from Pivotal DD Studies

An overview of AEs in the pooled DD studies is provided in Table 48. Similar to the NDD studies, most patients in the DD studies also experienced at least 1 AE. The percentage of patients experiencing at least one AE was similar in both groups. Roxadustat- and EPO-treated patients had similar rates of SAEs and fatal events. More patients in the roxadustat group experienced AEs leading to discontinuation.

Table 48: Pooled DD Studies: Summary of Overall Treatment-Emergent Adverse Events in Roxadustat- and Epoetin Alfa Groups

	Roxadustat N=1940	Epoetin Alfa N=1940
	n (%)	n (%)
Any AEs	1680 (86.6)	1669 (86.0)
Any SAEs	1080 (55.7)	1071 (55.2)
AEs leading to discontinuation	218 (11.2)	159 (8.2)
Any Fatal AEs	292 (15.1)	303 (15.6)
All-cause mortality ^a	207 (10.7)	232 (12.0)

Abbreviations: AE=adverse event; DD=dialysis-dependent; N=number of patients within treatment group; n=number of patients with the specified event; OT+7=on-treatment plus 7 days; OT+28=on-treatment plus 28 days; SAE=serious adverse event.

Note: Safety Population, OT+28 analyses, DD Pool: Studies 002, 063, 064.

6.6.2.1. Common Treatment-Emergent Adverse Events

The AE profile was generally similar for patients receiving roxadustat compared with those receiving the EPO. The summary of AEs with $\geq 5\%$ incidence is tabulated in Table 49. The most common AEs in both treatment groups were hypertension and diarrhea (both > 10%). Among other common events were headache, complications associated with vascular access, gastrointestinal events and infections.

^a Data shown from OT+7 analyses. Each death was adjudicated by a central adjudication committee that was blinded to treatment assignment.

Table 49: Pooled DD Studies: Summary of Treatment-Emergent Adverse Events (Incidence ≥ 5%) by Preferred Terms in Roxadustat and Epoetin Alfa Groups

Preferred Term	Roxadustat N=1940	Epoetin Alfa N=1940
	n (%)	n (%)
Any AE	1680 (86.6)	1669 (86.0)
Hypertension	253 (13.0)	229 (11.8)
Diarrhea	243 (12.5)	215 (11.1)
Headache	181 (9.3)	141 (7.3)
Arteriovenous fistula thrombosis	174 (9.0)	145 (7.5)
Pneumonia	175 (9.0)	193 (9.9)
Hypotension	170 (8.8)	147 (7.6)
Nausea	169 (8.7)	155 (8.0)
Vomiting	154 (7.9)	129 (6.6)
Arteriovenous fistula site complication	146 (7.5)	152 (7.8)
Cough	139 (7.2)	152 (7.8)
Hyperkalemia	138 (7.1)	138 (7.1)
Upper respiratory tract infection	136 (7.0)	114 (5.9)
Dyspnea	122 (6.3)	139 (7.2)
Fluid overload	120 (6.2)	128 (6.6)
Constipation	113 (5.8)	101 (5.2)
Pain in extremity	112 (5.8)	117 (6.0)
Muscle spasms	107 (5.5)	92 (4.7)
Pyrexia	105 (5.4)	101 (5.2)
Back pain	100 (5.2)	109 (5.6)
Dizziness	98 (5.1)	85 (4.4)
Urinary tract infection	97 (5.0)	102 (5.3)
Bronchitis	94 (4.8)	120 (6.2)
Viral upper respiratory tract infection	93 (4.8)	99 (5.1)
Fall	88 (4.5)	101 (5.2)
Atrial fibrillation	59 (3.0)	107 (5.5)

Abbreviations: AE=adverse event; DD=dialysis-dependent; OT+28=on-treatment plus 28 days. Note: Incidence ≥ 5%, Safety Population, OT+28 analyses, DD Pool: Studies 002, 063, 064.

6.6.2.2. Treatment-Emergent Adverse Events Leading to Discontinuation

As shown in Table 50, the incidence of AEs leading to discontinuation of treatment was 11.2% in roxadustat group and 8.2% in the EPO group. Cardiac arrest was the only single event reported in $\geq 1\%$ of patients leading to study discontinuation in both treatment groups.

Table 50: Pooled DD Studies: Summary of Treatment-Emergent Adverse Events (≥ 0.3%) Leading to Discontinuation by Preferred Terms in Roxadustatand Epoetin Alfa Groups

	Roxadustat N=1940	Epoetin Alfa N=1940
Preferred Term	n (%)	n (%)
AEs leading to discontinuation	218 (11.2)	159 (8.2)
Cardiac arrest	19 (1.0)	25 (1.3)
Sepsis	11 (0.6)	4 (0.2)
Septic shock	12 (0.6)	4 (0.2)
Acute myocardial infarction	10 (0.5)	6 (0.3)
Cardio-respiratory arrest	10 (0.5)	7 (0.4)
Nausea	8 (0.4)	0
Death	6 (0.3)	12 (0.6)
Hepatitis C	6 (0.3)	6 (0.3)
Myocardial Infarction	5 (0.3)	3 (0.2)
Multiple organ dysfunction syndrome	5 (0.3)	3 (0.2)
Sudden death	5 (0.3)	3 (0.2)
Hemorrhagic stroke	3 (0.2)	5 (0.3)

Abbreviations: AE=adverse event; DD=dialysis-dependent; OT+28=on-treatment plus 28 days. Note: Safety Population, OT+28 analyses, DD Pool: Studies 002, 063, 064.

7. DATA FROM SUPPORTIVE STUDY 610

7.1. General Safety Data from Supportive Study 610

The overall incidence of AEs observed in this study was comparable between treatment groups; 91.6% of patients in the roxadustat group and 92.5% of patients in the darbepoetin alfa group experienced AEs (Table 51). The incidence of SAEs was 64.7% in the roxadustat group versus 61.8% in the darbepoetin group; the incidence of AEs leading to death was 10.5% versus 11.6%, respectively. The percentage of patients with AEs leading to discontinuation was 7.7% in the roxadustat group compared to 3.8% in the darbepoetin group.

Table 51: Study 610: Overview of Treatment-emergent Adverse Events and Death (Safety Analysis Set)

	Roxadustat №323	Darbepoetin alfa N=293
Adverse Event	296 (91.6%)	271 (92.5%)
Serious Adverse Event	209 (64.7%)	181 (61.8%)
Adverse Event Leading to Death	34 (10.5%)	34 (11.6%)
Adverse Event Leading to Withdrawal of Treatment	25 (7.7%)	11 (3.8%)

The most common AEs were ESRD (33.4% in the roxadustat group vs 36.2% in the darbepoetin group), hypertension (29.7% vs 33.8%), decreased glomerular filtration rate (17.0% vs 16.7%), edema peripheral (15.2% vs 12.3%), and hyperkalemia (11.8% vs 14.3%) (Table 52).

Table 52: Study 610: Treatment-Emergent Serious Adverse Events (Safety Analysis Set)

	Roxadustat N=323	Darbepoetin alfa N=293
D 617	n (%)	n (%)
Preferred Term		
End-stage renal disease	108 (33.4)	106 (36.2)
Hypertension	96 (29.7)	99 (33.8)
Glomerular filtration rate decreased	55 (17.0)	49 (16.7)
Oedema peripheral	49 (15.2)	36 (12.3)
Hyperkalemia	38 (11.8)	42 (14.3)
Nausea	35 (10.8)	25 (8.5)
Viral upper respiratory tract infection	29 (9.0)	25 (8.5)
Diarrhea	28 (8.7)	30 (10.2)
Hyperphosphatemia	28 (8.7)	15 (5.1)
Pneumonia	25 (7.7)	22 (7.3)
Muscle spasms	25 (7.7)	15 (5.1)
Dyspnea	24 (7.4)	12 (4.1)
Bronchitis	22 (6.8)	18 (6.1)
Constipation	21 (6.5)	15 (5.1)
Vomiting	21 (6.5)	19 (6.5)
Urinary tract infection	21 (6.5)	27 (9.2)
Iron deficiency	21 (6.5)	25 (8.5)
Headache	21 (6.5)	12 (4.1)
Back pain	20 (6.2)	17 (5.8)
Pruritus	20 (6.2)	13 (4.4)
Insomnia	19 (5.9)	8 (2.7)
Anemia	14 (4.3)	19 (6.5)
Atrial fibrillation	18 (5.6)	12 (4.1)
Cardiac failure	18 (5.6)	18 (6.1)
Arthralgia	18 (5.6)	14 (4.8)
Dizziness	16 (5.0)	15 (5.1)

Abbreviations: N=number of patients in treatment group; n=number of patients with specified adverse event. Note: incidence \geq 5% in either group.

The overall incidence of AEs leading to treatment discontinuation was higher in roxadustattreated patients: 7.7% in the roxadustat group vs 3.8% in the darbepoetin group. ESRD was

the only AE leading to discontinuation that occurred in more than 1 patient in the roxadustat group (3 [0.9%] vs 2 [0.7%] patients in the darbepoetin group).

7.2. Safety Assessment of Specific Adverse Events from Supportive Study 610

Some imbalances in specific AEs were noted during the review of safety data from the NDD and DD pools. Table 53 presents a summary of those AEs for Study 610. VAT events were uncommon in Study 610, and the incidence of DVT and PE AEs was low in both groups. The incidence of infection AEs and SAEs were numerically lower and higher, respectively, for roxadustat compared to darbepoetin alfa; 2.2% of roxadustat patients died from infection, compared to 3.1% of darbepoetin patients. The event rate per 100 PY of convulsion AEs was 1.1 in the roxadustat group and 0.2 in the darbepoetin alfa group.

Table 53: Study 610: Summary of Specific Adverse Events

	Roxadustat	Darbepoetin Alfa
	N=323	N=293
	n (%)	n (%)
Vascular Access Thrombosis	10 (3.1)	7 (2.4)
Deep Vein Thrombosis	6 (1.9)	2 (0.7)
Pulmonary Embolism	2 (0.6)	3 (1.0)
Convulsions AEs (SMQ)	6 (1.9)	1 (0.3)
Convulsions SAEs (SMQ)	4 (1.2)	1 (0.3)
Infection/Infestation AE (SOC)	155 (48.0%)	150 (51.2)
Infection/Infestation SAE (SOC)	69 (21.4%)	52 (17.7%)
Infection Death	5 (1.5%)	5 (1.7%)

Abbreviations: MedDRA=Medical Dictionary for Regulatory Activities: N=number of patients in treatment group; n=number of patients with specified adverse event; SMQ=standardized MedDRA query; SOC=System Organ Class.

8. DATA FROM SUPPORTIVE STUDY 613

8.1. Efficacy Data from Supportive Study 613

A total of 838 patients were randomized into the study. All data from site 70051 (2 randomized patients) are excluded due to Good Clinical Practice violations. Therefore, a total of 836 patients were considered as ITT for statistical analysis, 415 to the roxadustat treatment group and 421 to the ESA group. Of these patients, a total of 834 patients (414 roxadustat, 420 ESA) who received at least one dose of study drug, were included in the Safety Population. A total of 833 patients (413 roxadustat, 420 ESA) received at least one dose of study drug and had baseline and at least one post-dose Hb assessment were included in the FAS population.

Baseline demographics in the Safety Population were notable, as the majority of patients receiving hemodialysis (91.5% vs 96.4%, respectively), with a median time since first dialysis of 2.89 and 2.97 years, respectively.

Duration of exposure was comparable between the roxadustat group and ESA group (median: 103.71 weeks in roxadustat vs, 103.14 in ESA). Total PEY was 637.2 for roxadustat vs 719.7 for ESA.

In general, the efficacy data from Study 613 was consistent with other pivotal studies (Studies 063, 064 and 002).

Primary Endpoint: Mean Change in Hb from Baseline to Mean Over Weeks 28 to 52

The LSMean of the treatment difference between roxadustat and ESA was 0.171 (95% CI: 0.082, 0.261).

IV Iron Supplementation

Mean monthly IV iron use was 12.0 mg in the roxadustat treatment group compared with 44.8 mg in the ESA group. The LSMean difference for roxadustat vs ESA was -31.9 mg (95% CI: -41.4, -22.4); this difference was statistically significant (p < 0.001), which was consistent with other individual studies.

RBC Transfusion

9.4% roxadustat-treated patients vs 12.9% ESA-treated patients received RBC transfusion with a HR of 0.867 (95% CI: 0.573, 1.313) in FAS during the efficacy emergent period (up to OT+7), demonstrating the non-inferiority between roxadustat and ESA.

8.2. Cardiovascular Safety Data from Supportive Study 613

Study 613 was an open-label Phase 3 DD CKD study with an active comparator group that was unique in the use of 2 different ESAs, EPO or darbepoetin alfa, as active controls; therefore, the CV safety data from this study are not included in the pooled CV safety DD CKD analyses. Baseline demographics are shown in Table 54. Please see the Executive Summary (Section 1.1) for a review of the design and limitations of Study 613.

Table 54: Study 613: Demographics and Baseline Characteristics

Parameter	Subgroup: Darbepoetin		Subgroup: Epoetin		
	Roxadustat	Darbepoetin Alfa	Roxadustat	Epoetin Alfa	
	(n=158)	(n=163)	(n=256)	(n=257)	
Sex, male, n (%)	97 (61.4)	98 (60.1)	148 (57.8)	137 (53.3)	
Race, White, n (%)	153 (96.8)	156 (95.7)	252 (98.4)	251 (97.7)	
Age, years, mean (SD)	61.1 (14.3)	61.8 (12.6)	61.0 (13.6)	61.9 (14.0)	
Weight, kg, mean (SD)	76.27 (15.75)	76.70 (16.65)	76.30 (15.99)	75.84 (17.65)	
BMI, kg/m ² , mean (SD)	26.70 (4.81)	26.81 (5.30)	26.97 (4.89)	27.05 (5.78)	
Hb, g/dL, mean (SD)	10.70 (0.60)	10.74 (0.64)	10.78 (0.63)	10.80 (0.61)	
LDL cholesterol, mmol/L, n (%)					
≤ULN	86 (54.4)	92 (56.4)	123 (48.0)	140 (54.5)	
> ULN	72 (45.6)	71 (43.6)	133 (52.0)	117 (45.5)	
Previous ESA dose/week, n (%)					
$<$ 25 μg darbepoetin alfa or $<$ 5000 IU epoetin	96 (60.8)	86 (52.8)	126 (49.2)	103 (40.1)	
25 to < 40 μg darbepoetin or 5000 to < 8000 IU epoetin	40 (25.3)	56 (34.4)	71 (27.7)	77 (30.0)	
40 to < 80 μg darbepoetin or 8000 to < 16000 IU epoetin	20 (12.7)	21 (12.9)	57 (22.3)	72 (28.0)	
≥ 80 µg darbepoetin or ≥ 16000 IU epoetin	2 (1.3)	0	2 (0.8)	5 (1.9)	
Baseline dialysis type, n (%)					
Hemodialysis	134 (84.8)	150 (92.0)	245 (95.7)	255 (99.2)	
Peritoneal dialysis	24 (15.2)	13 (8.0)	11 (4.3)	2 (0.8)	
Baseline hsCRP, nmol/L, n (%)					
≤ULN	83 (52.5)	87 (53.4)	127 (49.6)	139 (54.1)	
> ULN	75 (47.5)	76 (46.6)	129 (50.4)	118 (45.9)	
Dialysis vintage, years					
Mean (SD)	3.89 (3.65)	4.76 (4.23)	4.63 (4.46)	3.67 (3.17)	
Median (min, max)	2.75 (0.38, 20.88)	3.41 (0.33, 20.86)	3.14 (0.35, 27.04)	2.60 (0.34, 17.36)	
Iron repletion at baseline, n (%)					
Ferritin ≥ 100 ng/mL and TSAT $\geq 20\%$	135 (85.4)	144 (88.3)	220 (86.3)	222 (86.4)	
Blood pressure, mmHg, mean (SD)					
Systolic	134.6 (16.9)	136.7 (19.3)	135.5 (18.0)	137.0 (18.7)	

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Parameter	Subgroup: Darbepoetin		Subgroup: Epoetin	
	Roxadustat	Darbepoetin Alfa	Roxadustat	Epoetin Alfa
Diastolic	75.5 (10.6)	74.6 (11.3)	75.1 (11.3)	74.1 (11.2)
History of cardiovascular, cerebrovascular, or thromboembolic diseases, n (%)	55 (34.8)	70 (42.9)	114 (44.5)	131 (51.0)
History of diabetes, n (%)	43 (27.2)	52 (31.9)	61 (23.8)	81 (31.5)

Abbreviations: BMI=body mass index; ESA=erythropoiesis-stimulating agent; Hb=hemoglobin; hsCRP=high-sensitivity C-reactive protein; LDL=low-density lipoprotein; max=maximum; min=minimum; OT+28=on-treatment plus 28 days; SD=standard deviation; TSAT=transferrin saturation; ULN=upper limit of normal. Note: Safety Population; OT+28 analyses.

Table 55 and Figure 71 show the CV safety data: MACE, MACE+, and ACM from Study 613 using the Cox proportional hazards model during OT+7 evaluation window.

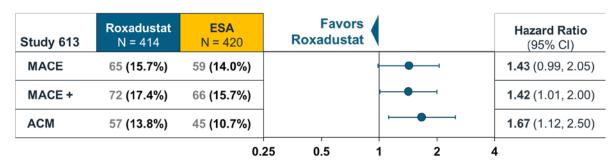
Table 55: Descriptive Statistics of MACE, MACE+, and ACM of Study 613

MACE MACE+		CE MACE+		CE+	A(CM
OT+7	Roxadustat	EPO / Darbe	Roxadustat	EPO / Darbe	Roxadustat	EPO / Darbe
Study 613	(n=414)	(n=420)	(n=414)	(n=420)	(n=414)	(n=420)
Total PEY	637.2	719.7	637.2	719.7	637.2	719.7
# of patients with events	65	59	72	66	57	45
Incidence / 100 PEY	10.2	8.2	11.3	9.2	8.9	6.3

Abbreviations: ACM=all-cause mortality; Darbe=darbepoetin alfa; DD=dialysis-dependent; EPO=epoetin alfa; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalizations for unstable angina or congestive heart failure; OT+7=on-treatment plus 7 days; PEY=patient exposure years. Note: Study 0613: randomized patients who took any dose of study medication in the DD study 0613.

Note: Active control is erythropoietin-stimulating agent: epoetin alfa or darbepoetin alfa.

Figure 71: Study 613: Forest Plot of MACE, MACE+, and ACM



Abbreviations: ACM=all-cause mortality; CI=confidence interval; DD=dialysis-dependent; ESA=erythropoiesis-stimulating agent; HR=hazard ratio; MACE=major adverse cardiovascular event (all-cause mortality, myocardial infarction, and stroke); MACE+=MACE, plus hospitalizations for unstable angina or congestive heart failure; OT+7=on-treatment plus 7 days.

Note: Study 613: randomized patients who took any dose of study medication in the DD Study 613.

Note: Active control is erythropoietin-stimulating agent: epoetin alfa or darbepoetin alfa.

Note: OT+7.

8.3. General Safety Data from Supportive Study 613

Study 613 general safety results were not pooled with the other Phase 3 pivotal dialysis studies as advised by FDA. The overall summary of AEs during the treatment period and within 28 days of the last dose of study medication are tabulated in Table 56. The overall incidence of AEs was similar between the treatment groups: 86.7% of patients in the roxadustat group and 86.0% in the ESA group. The percentage of patients with SAEs was 50.7% in the roxadustat group and 45.0% in the ESA group. The incidence of AEs leading to death was 16.2% in the roxadustat group compared to 13.1% in the ESA group. The percentage of patients with AEs leading to discontinuation of study medication was higher in the roxadustat group: 8.5% for roxadustat group vs 3.8% for ESA group.

Table 56: Study 613: Overview of Adverse Events and Death

	Roxadustat N=414	ESA N=420
	n (%)	n (%)
Any AE	359 (86.7)	361 (86.0)
Serious AE	210 (50.7)	189 (45.0)
AE leading to death	67 (16.2)	55 (13.1)
AE leading to withdrawal of treatment	35 (8.5)	16 (3.8)
Death during the safety emergent period (OT+28)	64 (15.5)	51 (12.1)

Abbreviations: AE=adverse event; ESA=erythropoiesis-stimulating agent; N=number of patients in treatment group; n=number of patients with specified AE.

The summary of AEs with $\geq 5\%$ incidence during the treatment period and within 28 days of the last dose of study medication are tabulated in Table 57. The most common AEs were hypertension (17.9% in the roxadustat vs 18.8% in the ESA group), AVF thrombosis (12.1% vs 7.4%) [AVF site complication (5.6% vs 5.0%)], headache (8.7% vs 6.9%), diarrhea (8.5% vs 8.3%) and bronchitis (8.0% vs 6.9%).

Table 57: Study 613: Roxadustat AEs (Incidence ≥ 5%) by Preferred Term Compared to Erythropoietin-Stimulating Agents

	Roxadustat	ESA
Preferred Term	N=414 n (%)	N=420 n (%)
Any AEs	359 (86.7%)	361 (86.0%)
Hypertension	74 (17.9%)	79 (18.8%)
Arteriovenous fistula thrombosis	50 (12.1%)	31 (7.4%)
Headache	36 (8.7%)	29 (6.9%)
Diarrhea	35 (8.5%)	35 (8.3%)
Bronchitis	33 (8.0%)	29 (6.9%)
Hypotension	33 (8.0%)	27 (6.4%)
Iron deficiency	30 (7.2%)	51 (12.1%)
Nausea	29 (7.0%)	8 (1.9%)
Viral upper respiratory tract infection	29 (7.0%)	39 (9.3%)
Pneumonia	23 (5.6%)	27 (6.4%)
Arteriovenous fistula site complication	23 (5.6%)	21 (5.0%)
Hyperparathyroidism secondary	22 (5.3%)	16 (3.8%)
Anemia	21 (5.1%)	16 (3.8%)
Atrial fibrillation	20 (4.8%)	25 (6.0%)
Muscle spasms	15 (3.6%)	33 (7.9%)
Upper respiratory tract infection	14 (3.4%)	22 (5.2%)
Fall	13 (3.1%)	21 (5.0%)

Abbreviations: AE=adverse event; ESA=erythropoiesis-stimulating agent; N=number of patients in treatment group; n=number of patients with the specified event; OT+28=on-treatment plus 28 days.

Note: Medical Dictionary for Regulatory Activities (MedDRA) coding dictionary version 20.0.

Note: Patients with more than one event in a category are counted only once for that category.

Note: OT+28.

The overall incidence of AEs leading to treatment discontinuation was higher in the roxadustat-treated patients; 8.5% in the roxadustat vs 3.8% in the ESA group. Individual AE leading to treatment discontinuation preferred terms were uncommon, with only acute coronary syndrome (2 [0.5%] vs 0 patients), acute myocardial infarction (2 [0.5%] vs 1 [0.2%]), cardiac arrest (0 vs 3 [0.7%]), death (2 [0.5%] vs 1 [0.2%]), sudden death (3 [0.7%] vs 0), sepsis (2 [0.5%] vs 0) and anxiety (2 [0.5%] vs 0) occurring in more than 1 patient in either treatment group.

8.4. Safety Assessment of Specific Adverse Events from Supportive Study 613

Some imbalances in specific AEs were noted during the review of safety data from the NDD and DD pools (Section 1.6.3). Table 58 presents a summary of those AEs for Study 613. A

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greater proportion of patients in the roxadustat treatment group had VAT compared with the ESA treatment group. Eight patients had DVT AEs in the roxadustat group and none in the ESA group; in the roxadustat group, 3 patients had PE compared with 1 in the ESA group. The rate of seizure AEs was low in the roxadustat and ESA groups; 2 roxadustat-treated patients and 3 ESA-treated patients experienced seizure AEs during the study. The incidence of infection AEs was similar in the roxadustat and ESA treatment groups. While the incidence rate of infection SAEs was higher in the roxadustat group compared to ESA, the rate of adjudicated infection death was similar in the 2 groups.

Table 58: Study 613: Summary of Specific Adverse Events

	Roxadustat	ESA
	N=414	N=420
	n (%)	n (%)
Vascular Access Thrombosis	49 (11.8)	36 (8.6)
Deep Vein Thrombosis	8 (1.9)	0 (0.0)
Pulmonary Embolism	3 (0.7)	1 (0.2)
Convulsions AEs (SMQ)	2 (0.5)	3 (0.7)
Convulsions SAEs (SMQ)	1 (0.2)	3 (0.7)
Infection/Infestation AE (SOC)	185 (44.7)	192 (45.7)
Infection/Infestation SAE (SOC)	82 (19.8)	66 (15.7)
Infection Death	12 (2.9)	11 (2.6)

Abbreviations: AE=adverse event; MedDRA=Medical Dictionary for Regulatory Activities; N=number of patients in treatment group; n=number of patients with specified event; OT+28=on-treatment plus 28 days; SAE=serious adverse event; SMQ=standardized MedDRA query; SOC=System Organ Class.

9. SAFETY DATA FROM OTHER PHASE 3 CKD STUDIES

A total of 16 Phase 3 studies have been completed. Three NDD (Studies 001, 060, 608) and 3 DD studies (Studies 002, 063, 064) have been pooled, respectively, and have been presented in this document. Safety data from 2 global studies (Studies 610 and 613) were considered supportive and have been presented in Section 7 and Section 8, respectively. This section provides a summary of safety data from the remaining 8 studies (3 NDD studies; 5 DD studies). These were local studies conducted in Japan and China to support regulatory approval in these 2 countries, respectively.

9.1. Japan Studies

Six Phase 3 studies sponsored by Astellas Pharma were completed in Japan; 2 studies in NDD population (Studies 1517-CL-0310, 1517-CL-0314) and 4 studies in DD population (Studies 1517-CL-0302, 1517-CL-0307, 1517-CL-0308, 1517-CL-0312). A total of 1,028 patients have participated in these studies. The clinical study reports were submitted to the FDA.

9.1.1. Study 1517-CL-0310 (NDD)

This was a Phase 3 randomized open-label, active-controlled study to evaluate the efficacy and safety of roxadustat in the treatment of anemia in patients with NDD CKD (N=332). The incidence of AEs was 78.6% (103/131 patients) in the roxadustat (comparative) group, 70.2% (92/131 patients) in the darbepoetin alfa (comparative) group, and 77.1% (54/70 patients) in the roxadustat (referential) group. AEs occurring in \geq 5% of patients in any treatment group included nasopharyngitis, CKD, hyperkalemia, and hypertension. The incidence of all the events in the roxadustat (comparative) group was similar to or lower than that in the darbepoetin alfa (comparative) group. The incidence of SAEs was 17.6% in the roxadustat (comparative) group, 13.0% in the darbepoetin alfa (comparative) group, and 12.9% in the roxadustat (referential) group. In the roxadustat (comparative) group, no patients died during the study. Deaths were reported in 1 patient (due to gastrointestinal necrosis) in the darbepoetin alfa (comparative) group and 2 patients (due to PE and myocardial ischemia) in the roxadustat (referential) group. In conclusion, roxadustat was well-tolerated demonstrating an AE profile comparable to darbepoetin alfa.

9.1.2. Study 1517-CL-0314 (NDD)

This was a Phase 3 randomized open-label, noncomparative study to evaluate the efficacy and safety of roxadustat in ESA-untreated patients with renal anemia (N=99). The incidence of AEs was 62.6% (62/99 patients) in total. The common (incidence \geq 5%) AEs were nasopharyngitis (20.2%), hypertension (6.1%), and diarrhea and hyperkalemia (5.1% each). The incidence of serious AE was 11.1% (11/99 patients) in total. The incidence of AEs leading to withdrawal of treatment was 6.1% (6/99 patients) in total. The incidence of drug-related AEs leading to withdrawal of treatment was 2.0% (2/99 patients) in total. No deaths were observed. In conclusion, roxadustat was well-tolerated and was consistent with other completed studies.

FibroGen

9.1.3. Study 1517-CL-0302 (DD)

This was a Phase 3 randomized multicenter, open-label, non-comparative study of the treatment of anemia in patients with CKD (N=56). The overall incidence of AEs was 87.5% (49/56 patients). The incidence of AEs was similar between the roxadustat treatment groups based on dose. The most common (incidence $\geq 5\%$) AEs in all the treatment groups were nasopharyngitis, back pain, catheter site infection, diarrhea, vomiting, abdominal pain, conjunctivitis, constipation, nausea and pruritus. The incidence of these events except for back pain and conjunctivitis in the pooled ESA-treated group was higher than that in the pooled ESA-untreated group. All AEs in all the treatment groups were mild or moderate in severity. No severe AEs were reported in any treatment group and there were no deaths in this study. A SAE which occurred in 2 or more patients in total was peritonitis (3.6%, 2/56 patients). One patient taking pravastatin experienced serious AE of rhabdomyolysis which was assessed as possibly related to roxadustat. In addition, to the roxadustat and pravastatin, febuxostat was also considered a suspect medication. Overall, roxadustat was well-tolerated demonstrating an AE profile similar to the underlying population of patients with anemia and CKD.

9.1.4. Study 1517-CL-0307 (DD)

This was a Phase 3 randomized multicenter, 2-arm parallel, double-blind, active comparator (darbepoetin alfa) conversion study of intermittent oral dosing of roxadustat in patients with DD CKD with anemia (N=303). The incidence of AEs was 86.0% (129/150 patients) in the roxadustat group and 82.9% (126/152 patients) in the darbepoetin alfa group. The most common (incidence > 5% in any arm) AEs were nasopharyngitis, shunt stenosis, diarrhea, contusion and vomiting. Of these, the events occurring more frequently in the roxadustat group compared with the darbepoetin alfa group were nasopharyngitis and vomiting. The incidence of SAEs was 20.7% (31/150 patients) in the roxadustat group and 14.5% (22/152 patients) in the darbepoetin alfa group. SAEs observed in 2 or more patients in the roxadustat group were shunt stenosis (4.0%, 6/150 patients), shunt occlusion (2.0%, 3/150 patients), cellulitis and DVT (1.3%, 2/150 patients each). Two deaths (1.3%, 2/150) were reported in the roxadustat group. One in a 64-year-old male patient that was on dialysis for 41 years and had a medical history of acute pericarditis and chronic heart failure died from acute myocardial infarction; the second case in a 75-year-old male patient with a history of hypertension, angina pectoris, hyperkalemia, and dyslipidemia who died from cardiopulmonary arrest due to congestive cardiac failure.

9.1.5. Study 1517-CL-0308 (DD)

This was a Phase 3 multicenter, randomized, 2-arm, open-label study of intermittent oral dosing of roxadustat in erythropoiesis-stimulating agent-naive patients with DD CKD with anemia (N=75). The incidence of AEs was 86.5% (21/37 patients), 94.7% (36/38 patients), and 90.7% (68/75 patients) in the roxadustat 50 mg, 70 mg groups, and total, respectively. The most common (incidence \geq 5%) AEs were nasopharyngitis (20.0%), dermatitis contact (13.3%), shunt occlusion (9.3%), constipation, shunt stenosis and hyperphosphatemia (6.7% each), and diarrhea, vomiting, eczema, contusion, back pain and insomnia (5.3% each). The incidence of SAEs was 29.3% (22/75 patients) in total. SAEs observed in more than 1 patient were shunt occlusion 6.7% (5/75 patients) and cardiac failure congestive 2.7%

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(2/75 patients). No deaths were observed. The 50 mg starting dose group tended to be associated in general with a numerically lower AE rate compared to the 70 mg starting dose group. In conclusion, roxadustat was well-tolerated demonstrating an AE profile similar to the underlying population of patients with anemia and CKD.

9.1.6. Study 1517-CL-0312 (DD)

This was a long-term study of intermittent oral dosing of roxadustat in patients with DD CKD with anemia converted from ESA treatment (N=163). The overall incidence of AEs was 95.7% (156/163 patients) in total. The common (incidence > 5%) AEs in total were nasopharyngitis (52.8%), diarrhea (11.0%), vomiting (10.4%), contusion (9.8%), shunt stenosis, back pain (7.4% each), constipation, shunt occlusion (6.1% each), dental caries, and headache (5.5% each). According to the analysis for onset of AEs by time interval, there was no increase in the incidence of AEs dependent on the roxadustat administration period. The incidence of SAEs was 28.2% (46/163 patients) in total. SAEs observed in 2 or more patients were shunt occlusion (5.5%, 9/163 patients), angina pectoris, pneumonia (1.8%, 3/163 patients each), myocardial ischemia, shunt stenosis, arteriogram coronary, skin ulcer, and peripheral arterial occlusive disease (1.2%, 2/163 patients each). The incidence of deaths was 1.2% (2/163 patients) in total, and no relationships with roxadustat were found. A 79year-old male patient died of pancreatic carcinoma and 67-year-old male patient died of hemorrhagic shock which was attributed to bleeding from multiple gastric and duodenal ulcers. The cause of the ulcers was unknown; however, it was considered that sepsis had a major influence. In conclusion, roxadustat was well-tolerated demonstrating an AE profile similar to the underlying population of patients with anemia and CKD.

9.2. China Studies

Two Phase 3 studies sponsored by FibroGen China were completed in China; one in NDD population (Study FGCL-4592-808) and one in DD population (Study FGCL-4592-806). A total of 456 patients have participated in these studies. The clinical study reports were submitted to the FDA.

9.2.1. Study FGCL-4592-808 (NDD)

This Phase 3 randomized, multicenter, double-blind, placebo-controlled study of the treatment of anemia in patients with NDD CKD (N=152) had an 8-week double-blind treatment period with roxadustat or placebo, an 18-week open-label treatment period and an extension period for 26 additional weeks for the patients who were randomized to roxadustat.

During the double-blind treatment period, 69 (68.3%) patients in the roxadustat arm and 38 (74.5%) patients in the placebo arm reported AEs. The most commonly reported AEs higher on the roxadustat treatment arm than placebo included hyperkalemia, metabolic acidosis, peripheral edema, and hypertension. There was no specific safety signal or clustering of SAEs detected in either arm, and no deaths were reported during this study period.

During the 18-week open-label treatment period, a combined total of 112 (87.5%) patients reported AEs. The most commonly reported AEs were ESRD/CKD, hyperkalemia, hypertension, upper respiratory tract infection, and metabolic acidosis, events commonly

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encountered in this patient population. A total of 33 patients (25.8%) reported at least one SAE during this period of the study. Two deaths (2.4%) were reported during this study period: a 69-year-old female developed a sudden loss of consciousness at home without complaints of discomfort prior to the event and died before reaching hospital and a 60-year-old female died from post-operative retroperitoneal hemorrhage secondary to a surgical complication. Both deaths were considered by the investigators as not related to study drug.

In the 26-week extension period, 20 (87%) reported AEs. The most common AEs were hyperkalemia, metabolic acidosis, upper respiratory tract infection, hypertension, and iron deficiency. The AEs reported in the 52-week extension treatment period were similar to the initial treatment period. During the extension treatment period, 8 (34.8%) of patients reported treatment-emergent SAEs. No deaths occurred during the extension treatment period.

Overall, roxadustat was evaluated to be safe and well-tolerated in this NDD patient population.

9.2.2. Study FGCL-4592-806 (DD)

This Phase 3 randomized, multicenter, open-labeled, active-controlled study in patients with anemia associated with CKD who were on dialysis (N=304) had a 26-week treatment period and an extension period for up to 26 additional weeks for the patients who were randomized to roxadustat.

During the initial treatment period, a total of 160 (78.4%) patients in the roxadustat arm reported AEs, while 64 (64.0%) in the EPO arm reported AEs. The most common AEs that were reported in greater proportion in the roxadustat arm over the EPO arm were events of upper respiratory tract infection, hyperkalemia, chest discomfort, vomiting, and asthenia. The roxadustat-treated patients reported a slightly higher proportion (15.7%, including 1.5% hospitalized for routine dialysis treatment) of SAEs compared to the EPO-treated patients (10.0%). However, there was no important safety signal detected in the roxadustat arm.

Among 32 patients reported with SAEs in the roxadustat arm, 3 deaths occurred during the initial treatment period: a 65-year-old male died from an acute myocardial infarction, a 61-year-old male died from gastrointestinal hemorrhage and a 57-year-old female, died from cardiac failure. All 3 deaths were assessed by the investigators and by the Sponsor to be unrelated to study medication.

In the extension treatment period, a total of 96 (86.5%) patients reported AEs, most of which were mild or moderate in severity. The most common AEs reported were upper respiratory tract infection (31.5%), hypertension (15.3%), and hyperkalemia (9.9%). Two deaths were reported: one 64-year-old male who died from gastrointestinal perforation prior to surgical intervention, and another 52-year-old female with a history of hypertension who died from cerebral hemorrhage. None of these 2 deaths were considered related to study drug. Seventeen (15.3%) patients reported SAEs, the most common being AVF site stenosis/thrombosis (5 patients) in hemodialysis patients. Two peritoneal dialysis patients reported peritonitis.

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Overall, roxadustat was considered to be safe and well-tolerated in this DD patient population.

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10. DISPOSITION TABLES

A total of 4,270 eligible patients from the 3 pivotal Phase 3 studies were randomized to roxadustat (N=2,386) or placebo (N=1,884) and received at least 1 dose of study treatment. Substantially more patients in the placebo group discontinued study treatment prematurely compared to roxadustat. The main reasons for discontinuation were withdrawal by patient, AEs, and development of study specific discontinuation criteria related to requirement for rescue therapy (ie, RBC transfusion, ESA use, and IV iron supplementation) due to lack of efficacy of study drug (Table 59). These imbalances in disposition led to greater duration of treatment in the roxadustat group and retention of higher-risk patients (eg, those with low eGFR and those who required dialysis initiation) in the roxadustat group compared to the placebo group over time, leading to bias and confounding in on-treatment safety analyses.

Table 59: Pooled NDD Studies: Reasons for Discontinuation

NDD (Studies 608, 060, 001)	Roxadustat	Placebo
ITT Population	2391	1886
Main Reasons for Discontinuation, n (%):		
Adverse Event	150 (6.3)	83 (4.4)
Death ^b	81 (3.4)	30 (1.6)
Development of Study Specific Discontinuation Criteria ^a	76 (3.2)	252 (13.4)
Dialysis Initiation	23 (1.0)	11 (0.6)
Kidney Transplant	24 (1.0)	9 (0.5)
Lack of Efficacy	7 (0.3)	74 (3.9)
Lost to Follow-up	33 (1.4)	8 (0.4)
Non-compliance to Protocol	23 (1.0)	20 (1.1)
Not Reported	2 (0.1)	3 (0.2)
Physician Decision	49 (2.1)	67 (3.6)
Pregnancy	1 (0.0)	0
Site Terminated by Sponsor	2 (0.1)	1 (0.1)
Study Terminated by Sponsor	2 (0.1)	0
Patient Decision	250 (10.5)	390 (20.7)
Patient Relocated/Moved (or Lost to Follow-up)	6 (0.3)	10 (0.5)
Withdrawal by Parent/Guardian	1 (0.0)	1 (0.1)
Withdrawal by Patient	143 (6.0)	143 (7.6)
Other	28 (1.2)	13 (0.7)

Abbreviations: ITT=intent-to treat; NDD=non-dialysis-dependent.

A total of 1943 patients were randomized in the roxadustat group and 1947 in the EPO group for a total of 3,890 patients who were included in the ITT set. A total of 1940 patients in each group received at least 1 dose of study drug and were included in the Safety Analysis Set. The ID-DD subpopulation consisted of 1,530 patients, and the SDD subpopulation consisted of 2,360 patients.

The main reasons for premature treatment discontinuation were withdrawal by patient, AEs, death, and kidney transplant (Table 60).

^a In Study 001, patients reported "study specific discontinuation criteria" were patients who were discontinued from study drug for initiating dialysis during the study, and for whom there was a need for rescue with erythropoietin analogue.

^b In Table 36 in Section 6.4.1 patients who died while on treatment were considered to have completed treatment and completed the study.

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Table 60: Pooled DD Studies: Patient Disposition

	DD Pool		ID-DD Pool		SDD Pool	
	Roxa	Epoetin	Roxa	Epoetin	Roxa	Epoetin
ITT Population	1943	1947	760	770	1183	1177
Reasons for discontinuation, n (%)						
Withdrawal by patient	213 (11.0)	166 (8.5)	56 (7.3)	62 (8.1)	157 (13.4)	104 (8.9)
Adverse event	110 (5.7)	54 (2.8)	35 (4.6)	25 (3.3)	75 (6.4)	29 (2.5)
Deatha	141 (7.3)	129 (6.6)	69 (9.1)	61 (8.0)	72 (6.1)	68 (5.8)
Kidney transplant	115 (5.9)	147 (7.6)	26 (3.4)	33 (4.3)	89 (7.5)	114 (9.7)

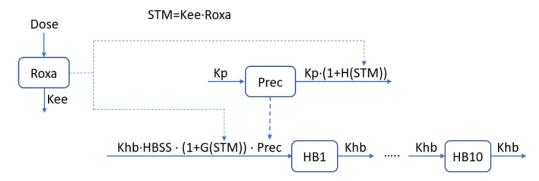
Abbreviations: DD=dialysis-dependent; ID-DD=incident dialysis-dependent; ITT=intent-to-treat; SDD=stable dialysis-dependent; Roxa=roxadustat.

Note: Intent-to-treat analysis set.

^a In Table 40 in Section 6.4.2 patients who died while on treatment were considered to have completed treatment and completed the study.

11. DOSE MODIFICATION MODEL

Figure 72: Roxadustat Starting Dose Modifications



Roxadustat acts at two points in the model via the effect compartment

Hemoglobin synthesis stimulus: $G(STM) = \frac{EMAX \cdot STM^{Gamma}}{STM^{Gamma} + EC50^{Gamma}}$

• Pre-curser depletion stimulus : $H(STM) = \frac{Dcal \cdot EMAX \cdot STM^{Gamma}}{STM^{Gamma} + \tau \cdot EC50^{Gamma}}$

Abbreviations: Dcal=depletion calibration; EC50=concentration that achieves 50% of the effect; EMAX=maximum effort; HB=hemoglobin; Kee=roxadustat elimination rate constant; Khb=rate constant for elimination of Hb; Kp=precursor production rate constant; Prec=Hb precursor; Roxa=roxadustat.

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EXHIBIT XX

FDA CRDAC

July 15 2021 FOOD AND DRUG ADMINISTRATION CENTER FOR DRUG EVALUATION AND RESEARCH CARDIOVASCULAR AND RENAL DRUGS ADVISORY COMMITTEE (CRDAC) Virtual Meeting Thursday, July 15, 2021 9:30 a.m. to 5:33 p.m.

FDA CRDAC July 15 2021 2 1 Meeting Roster DESIGNATED FEDERAL OFFICER (Non-Voting) 2 Joyce Yu, PharmD 3 4 Division of Advisory Committee and Consultant Management 5 Office of Executive Programs, CDER, FDA 6 7 CARDIOVASCULAR AND RENAL DRUGS ADVISORY COMMITTEE 8 9 MEMBERS (Voting) 10 Jacqueline D. Alikhaani, BA (Consumer Representative) 11 Volunteer and Advocate 12 American Heart Association 13 Los Angeles, California 14 15 16 C. Noel Bairey Merz, MD, FACC, FAHA, FESC 17 Director 18 Barbra Streisand Women's Heart Center Cedars-Sinai Medical Center 19 Los Angeles, California 20 21 22

July 15 2021 FDA CRDAC 3 Thomas D. Cook, PhD, MS, MA 1 Professor (Clinical Health Sciences) 2 Clinical Trials Program 3 4 Department of Biostatistics and Medical Informatics 5 University of Wisconsin-Madison 6 7 Madison, Wisconsin 8 9 Edward K. Kasper, MD, FACC, FAHA Director of Outpatient Cardiology 10 Johns Hopkins Medicine 11 E. Cowles Andrus Professor in Cardiology 12 Johns Hopkins School of Medicine 13 Baltimore, Maryland 14 15 Julia B. Lewis, MD 16 17

(Chairperson)

18 Professor of Medicine

19 Division of Nephrology

Vanderbilt Medical Center 20

21 Nashville, Tennessee

22

FDA CRDAC

July 15 2021

4

David J. Moliterno, MD 1 Professor and Chairman 2 Department of Internal Medicine 3 4 University of Kentucky Medical Center Lexington, Kentucky 5 6 Christopher M. O'Connor, MD, MACC, 7 FESC, FHFA, FHFSA 8 Professor of Medicine, Duke University 9 President and Executive Director 10 Inova Heart and Vascular Institute 11 Falls Church, Virginia 12 13 Ravi I. Thadhani, MD, MPH 14 15 Chief Academic Officer Massachusetts General Brigham 16 Professor of Medicine and Dean for Academic 17 18 Programs Mass General Brigham Harvard Medical School 19 Boston, Massachusetts 20 21 22

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ACTING INDUSTRY REPRESENTATIVE TO THE COMMITTEE 1 (Non-Voting) 2 David G. Soergel, MD 3 4 Global Head Cardiovascular, Renal and Metabolism Development 5 Novartis Pharma 6 7 East Hanover, New Jersey 8 TEMPORARY MEMBERS (Voting) 9 10 Leslie S. Cho, MD, FACC, FSCAI, FESC Section Head, Preventive Cardiology and 11 Rehabilitation 12 Professor of Medicine 13 Cleveland Clinic Lerner College of Medicine 14 15 Case Western Reserve Medical School Cleveland Clinic 16 Cleveland, Ohio 17 18 19 Paul T. Conway (Patient Representative) 20 21 Falls Church, Virginia 22

FDA CRDAC July 15 2021 6

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1
      Susan T. Crowley, MD, MBA, FASN
      Professor of Medicine (Nephrology)
2
      Yale University
3
4
      Director, National Kidney Disease &
5
      Dialysis Program
      Veterans Health Administration
6
      West Haven, Connecticut
7
8
9
      Milton Packer, MD
      Distinguished Scholar in Cardiovascular
10
      Medicine
11
      Baylor Heart and Vascular Institute
12
      Baylor University Medical Center
13
14
      Dallas, Texas
15
      Afshin Parsa, MD, MPH
16
      Senior Scientific Advisor and Program
17
18
      Director
19
      Division of Kidney, Urologic, and
      Hematologic Diseases
20
21
      NIDDK, NIH
22
      Bethesda, Maryland
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July 15 2021 FDA CRDAC 7 Thomas J. Wang, MD 1 Professor and Chair 2 Department of Internal Medicine 3 4 Donald W. Seldin Distinguished Chair University of Texas Southwestern 5 Medical Center 6 7 Dallas, Texas 8 9 FDA PARTICIPANTS (Non-Voting) Ellis F. Unger, MD 10 11 Director Office of Cardiology, Hematology, 12 Endocrinology and Nephrology (OCHEN) 13 Office of New Drugs (OND), CDER, FDA 14 15 Ann T. Farrell, MD 16 17 Director

18 Division of Non-Malignant Hematology (DNH)

19 OCHEN, OND, CDER, FDA

21

20

22

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1
      Saleh Ayache, MD
      Clinical Reviewer
2
      DNH, OCHEN, OND, CDER, FDA
3
4
5
      Jae Joon Song, PhD
      Statistical Reviewer
6
      Division of Biometrics VII
7
      Office of Biostatistics
8
      Office of Translational Sciences
9
10
      CDER, FDA
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1 PROCEEDINGS (9:30 a.m.)2 Call to Order 3 DR. LEWIS: Good morning and welcome. I 4 would like to remind everyone to please mute your 5 line when you are not speaking. For media and 6 7 press, the FDA press contact is Chanapa Tantibanchachai. Her email and phone number are 8 currently displayed. 9 My name is Julia Lewis, and I will be 10 chairing this meeting. I will now call the 11 July 15, 2021 meeting of the Cardiovascular and 12 Renal Drugs Advisory Committee to order. Dr. Joyce 13 Yu is the designated federal officer for this 14 meeting and will begin with introductions. 15 Introduction of Committee 16 DR. YU: Good morning. My name is Joyce Yu, 17 18 and I'm the designated federal officer for this 19 meeting. When I call your name, please introduce yourself by stating your name and affiliation. 20 21 We'll start with Ms. Alikhaani. MS. ALIKHAANI: Good morning. I'm 22

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Jacqueline Alikhaani. I live in Los Angeles.
1
     a heart patient and volunteered citizen scientist.
2
      I'm a community health volunteer with the American
3
4
     Heart Association and PCORI, the Patient-Centered
     Outcomes Research Institute, and the University of
5
     California, Los Angeles.
6
             DR. LEWIS:
7
                          Thank you.
             Dr. Bairey Merz?
8
9
             DR. BAIREY MERZ: Good morning. Noel Bairey
             I'm a clinical and investigative
10
     Merz.
      cardiologist at Cedars-Sinai Medical Center in Los
11
     Angeles, with the specialties of ischemic heart
12
      disease and women's heart disease.
13
             DR. YU: Thank you.
14
             Dr. Cook?
15
             DR. COOK: This is Thomas Cook. I'm a
16
     biostatistician at the University of
17
18
     Wisconsin-Madison, where I specialize in clinical
     trials.
19
             DR. YU: Thanks.
20
21
             Dr. Kasper?
             DR. KASPER: Good morning. Kevin Kasper.
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I'm a cardiologist at Johns Hopkins with interest
1
      in heart failure and heart transplantation.
2
3
             DR. YU: Thank you.
             Dr. Lewis?
4
             DR. LEWIS: Good morning. I'm Dr. Julia
5
            I'm a nephrologist at Vanderbilt
6
7
     University. Thank you.
             DR. LEWIS: Dr. Moliterno?
8
             DR. MOLITERNO: Hi. David Moliterno.
9
     professor of medicine and cardiologist at the
10
     University of Kentucky.
11
             DR. YU: Thanks.
12
             Dr. O'Connor?
13
             DR. O'CONNOR: Good morning. Chris O'Connor
14
             I'm a heart-failure cardiologist interested
15
      in heart-failure clinical trials and also serve as
16
     president of the Inova Heart and Vascular Institute
17
18
     health system outside Washington DC.
19
             DR. BAIREY MERZ: Dr. Thadhani?
             DR. THADHANI: Good morning. My name is
20
21
     Ravi Thadhani. I'm the chief academic officer at
     Mass General Brigham and a nephrologist by
22
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July 15 2021

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14
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1
      training.
                 Thank you.
                      Unfortunately, Dr. Abbott is not
             DR. YU:
2
      able to participate today, in today's meeting.
3
4
     had an emergency. So we'll move on to Dr. Cho.
              (No response.)
5
                      Dr. Cho, you're muted in the Adobe
6
     Connect. Would you mind unmuting?
7
              (Pause.)
8
             DR. CHO: Hi. Leslie Cho, professor of
9
     medicine, interventional cardiologist at Cleveland
10
     Clinic.
11
12
             DR. YU:
                      Thank you so much.
             Mr. Conway?
13
                          Hi. My name is Paul Conway.
14
             MR. CONWAY:
      serve as chair of Policy and Global Affairs at the
15
     American Association of Kidney Patients, and I'm a
16
      40-year kidney patient. Thank you.
17
18
             DR. YU: Dr. Crowley?
19
             DR. CROWLEY: Yes. Hi.
                                       I'm a nephrologist
      for the Veterans Health Administration and a
20
21
     professor of medicine at Yale University.
             DR. YU: Dr. Packer?
22
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DR. PACKER: Yes. I'm a cardiologist at
1
     Baylor University Medical Center with a focus on
2
      clinical trials. I guess I should just state for
3
4
     the record that there is a waiver in my name that
     has given me an extra degree. I do not have an MPH
5
     degree. So Joyce, I just wanted to put that in for
6
     the record.
7
             DR. YU: Thanks, Dr. Packer.
8
             DR. PARSA: Good morning. I'm Afshin Parsa.
9
      I'm a nephrologist and senior scientific advisor at
10
      the National Institutes of Health.
11
             DR. YU: Dr. Wang?
12
13
             DR. WANG: Hi. I'm Tommy Wang.
      cardiologist and chair of medicine at
14
     UT Southwestern Medical Center.
15
             DR. YU: Dr. Soergel?
16
             DR. SOERGEL: Good morning. David Soergel.
17
18
      I'm a pediatric cardiologist industry
19
      representative from Novartis.
             DR. YU: We'll move on to our FDA
20
21
     participants.
22
             Dr. Unger?
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I'm Ellis Unger.
1
             DR. UNGER:
                                             I'm a
     cardiologist and the director of the Office of
2
      Cardiology, Hematology, Endocrinology, and
3
4
     Nephrology in the Office of New Drugs, Center for
     Drug Evaluation and Research at FDA.
5
             DR. YU: Thanks.
6
             Dr. Farrell?
7
              (No response.)
8
                     Dr. Farrell, go ahead and unmute in
9
             DR. YU:
      the Adobe Connect at the top of your screen at the
10
     phone icon. I think you're muted there.
11
12
             DR. FARRELL:
                           Hello. My name is Ann
     Farrell. I'm a hematologist and medical
13
      oncologist, and I'm the division director of the
14
     Division of Non-Malignant Hematology in the Office
15
     of Cardiology, Hematology, Nephrology, and
16
     Endocrinology. Thank you.
17
18
             DR. YU:
                      Thanks, Dr. Farrell.
19
             Dr. Ayache?
             DR. AYACHE:
                          My name is Dr. Saleh Ayache.
20
21
      I'm a medical officer in the Division of
     Non-Malignant Hematology in the Office of
22
```

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Cardiology, Hematology, Endocrinology, and 1 Nephrology. 2 DR. YU: And finally, Dr. Jae Joon Song? 3 DR. SONG: Good morning. My name is Dr. Jae 4 Joon Song, and I am a statistical reviewer at the 5 FDA Center for Drug Evaluation and Research, Office 6 of Biostatistics. 7 DR. YU: I'll hand it over to you, 8 Dr. Lewis. 9 10 DR. LEWIS: Thank you. For topics such as those being discussed at 11 12 this meeting, there are often a variety of opinions, some of which are quite strongly held. 13 Our goal is that this meeting will be a fair and 14 open forum for discussion of these issues and that 15 individuals can express their views without 16 interruption. 17 18 Thus, as a gentle reminder, individuals will 19 be allowed to speak into the record only if recognized by the chairperson. We look forward to 20 21 a productive meeting. In the spirit of the Federal Advisory 22

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Committee Act and the Government in the Sunshine

Act, we ask that the advisory committee members

take care that their conversations about the topic

at hand take place in the open forum of the

meeting.

We are aware that members of the media are anxious to speak with the FDA about these proceedings, however, FDA will refrain from discussing the details of this meeting with the media until its conclusion. Also, the committee is reminded to please refrain from discussing the meeting topic during breaks or lunch. Thank you.

Dr. Joyce Yu will now read the Conflict of Interest Statement for the meeting.

Conflict of Interest Statement

DR. YU: The Food and Drug Administration is convening today's meeting of the Cardiovascular and Renal Drugs Advisory Committee under the authority of the Federal Advisory Committee Act of 1972.

With the exception of the industry representative, all members and temporary voting members of the committee are special government employees, SGEs,

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or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with federal ethics and conflict of interest laws, covered by but not limited to those found at 18 U.S.C. Section 208, is being provided to participants in today's meeting and to the public.

temporary voting members of this committee are in compliance with federal ethics and conflict of interest laws. Under 18 U.S.C. Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts when it is determined that the agency's need for a special government employee's services outweighs his or her potential financial conflict of interest, or when the interest of a regular federal employee is not so substantial as to be deemed likely to affect the integrity of the services

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20

which the government may expect from the employee. 1 Related to the discussions of today's 2 meeting, members and temporary voting members of 3 this committee have been screened for potential 4 financial conflicts of interest of their own as 5 well as those imputed to them, including those of 6 their spouses or minor children and, for purposes 7 of 18 U.S.C. Section 208, their employers. 8 interests may include investments; consulting; 9 expert witness testimony; contracts, grants, 10 CRADAs; teaching, speaking, writing; patents and 11 12 royalties; and primary employment. Today's agenda involves discussion of the 13 14 new drug application 213805, for the hypoxia inducible factor prolyl hydroxylase inhibitor, 15 roxadustat tablets, submitted by FibroGen, 16 Incorporated, for the treatment of anemia due to 17 18 chronic kidney disease in adult patients not on 19 dialysis and on dialysis. This is a particular matters meeting during which specific matters 20 21 related to FibroGen's NDA will be discussed. Based on the agenda for today's meeting and 22

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all financial interests reported by the committee members and temporary voting members, a conflict of interest waiver has been issued in accordance with 18 U.S.C. Section 208(b)(3) to Dr. Milton Packer. Dr. Packer's waiver involves stock holdings in affected firms.

The waiver allows this individual to participate fully in today's deliberations. FDA's reasons for issuing the waivers are described in the waiver document, which is posted on FDA's website at: https://www.fda.gov/advisory-committees/committees-and-meeting-materials/human-drug-advisory-committees.

Copies of the waiver may also be obtained by submitting a written request to the agency's Freedom of Information division, 5630 Fishers Lane, Room 1035, Rockville, Maryland, 20857, or requests may be sent via fax to 301-827-9267. To ensure transparency, we encourage all standing committee members and temporary voting members to disclose any public statements that they have made concerning the product at issue.

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With respect to FDA's invited industry 1 2 representative, we would like to disclose that Dr. David Soergel is participating in this meeting 3 4 as a non-voting industry representative, acting on behalf of regulated industry. Dr. Soergel's role 5 at this meeting is to represent industry in general 6 and not any particular company. Dr. Soergel is 7 employed by Novartis. 8 We would like to remind members and 9 temporary voting members that if the discussions 10 involve any other products or firms not already on 11 the agenda for which an FDA participant has a 12 13 personal or imputed financial interest, the participants need to exclude themselves from such 14 involvement, and their exclusion will be noted for 15 16 the record. FDA encourages all other participants to advise the committee of any financial 17 18 relationships that they may have with the firm at issue. 19 Thank you. DR. LEWIS: We will proceed with FDA opening 20 21 remarks from Dr. Ellis Unger. Dr. Unger? 22

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FDA Opening Remarks - Ellis Unger

DR. UNGER: Hi, and good morning, again, everyone. I'd like to welcome all of you to this advisory committee meeting and in advance of the proceedings, I'd like to take the opportunity to thank the committee, the patient and industry reps, registered public speakers, the applicant, and last but not least, the patients and interested parties who are listening online for all your efforts and interest in this application.

We'll be discussing roxadustat for the treatment of anemia of chronic kidney disease, and it's a complex application. It raises several important issues. We convened this meeting because we sincerely seek the committee's opinions and advice here. As usual, I'll remind you that although your votes are important, the discussion and the rationale behind your votes will likely be even more valuable to us.

Now typically, the division director would make the remarks here, but Dr. Ann Farrell has allowed me the honor of speaking in her place

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because, as she puts it, I have a passion for these patients and these therapies.

I've always felt that patients with chronic kidney disease deserve a better deal. Almost exactly 20 years ago, when I was fairly new at FDA, I was the medical officer who reviewed the application for darbepoetin alfa, which we approved, and it's still marketed for the anemia of chronic kidney disease.

When I was just beginning that review, I remember my supervisor telling me that we already knew that the drug could be titrated to raise the hemoglobin level to its target. That wasn't the issue. The question was whether it could do so safely. And that's exactly the same question we face today, but now the question is for the first drug in an entirely new class, and it's the first oral drug for this indication.

The applicant's hope was that roxadustat would be as effective as the approved erythropoiesis stimulating agents, and I think that we all hoped perhaps it would be safer. The

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development program was robust. It was aimed to show roxadustat's efficacy and safety in patients who were on and not on dialysis.

The main studies in the dialysis population were combined and the main studies in the non-dialysis populations were combined, and meta-analyses were conducted to examine major adverse cardiovascular events in both of these populations.

Now you'll see that the results of these analyses are somewhat difficult to interpret, as they're sensitive to the duration that patients were followed after they discontinued treatment, and we'll be discussing this in some detail.

In the non-dialysis population, patients with significant anemia were randomized to placebo, and not surprisingly, there were many more discontinuations in the placebo groups than in the roxadustat groups, which to some extent confounded the safety analyses.

With respect to the standard analyses of safety, there were greater rates of some important adverse events with roxadustat than even epoetin

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alfa, thrombotic events in particular. The absolute risks per patient-year are not large, but the adverse events are obviously important. Some of those events were thrombosis of vascular access, which is a lifeline in dialysis patients.

Twenty years ago, I advanced a theory, based on my analyses within the darbepoetin alfa application, that a rapid rate of rise in hemoglobin might lead to adverse events, maybe secondary to increases in blood viscosity. Our biometrics team performed these analyses for roxadustat, and indeed they found associations between hemoglobin rate of rise and thrombotic events. But you'll see that these analyses are based on, really, very small numbers of adverse events and are, at best, associations.

In recent discussions with the applicant, they've embraced the view that roxadustat's risks may be reduced with a more conservative dosing strategy that would limit the hemoglobin rate of rise, but I'll note that the rate-of-rise hypothesis remains unproven, and their plan is

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untested, but we'll discuss it.

Finally and importantly, I want to emphasize that our approval standards are based on demonstration that a drug is safe and effective and that there are adequate instructions for use. generally don't reject drugs based on comparative effectiveness or comparative safety, although we do consider the benefits and risks of new drugs within the context of available therapies.

So with that, I'll cede the floor, the virtual floor, for your presentations and deliberations. And again, I thank you so much for your participation.

> DR. LEWIS: Thank you, Dr. Unger.

Both the Food and Drug Administration and the public believe in a transparent process for information gathering and decision making. ensure such transparency at the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation.

For this reason, the FDA encourages all

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participants, including FibroGen's non-employee presenters, to advise the committee of any financial relationships they may have with the sponsor such as consulting fees, travel expenses, honoraria, and interest in the sponsor, including equity interests and those based upon the outcome of the meeting.

Likewise, FDA encourages you at the beginning of your presentation to advise the committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your presentation, it will not preclude you from speaking.

 $\label{eq:weighted_problem} \mbox{We will now proceed with presentations from} \\ \mbox{FibroGen.}$

Applicant Presentation - Wayne Frost

DR. FROST: Good morning, members of the Cardiovascular and Renal Drugs Advisory Committee and the FDA. I'm Wayne Frost, senior vice president of regulatory affairs at FibroGen, and we're excited to be here today with our partner

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AstraZeneca to share the data for roxadustat for the treatment of anemia in patients with chronic kidney disease.

Roxadustat is a novel, oral therapy to treat patients with anemia of CKD and the first major innovation in the management of this condition in 30 years. Patients with anemia of CKD need options beyond existing therapies.

Anemia is a common and burdensome complication of CKD that is associated with undesirable clinical outcomes. Many patients are underserved, especially those who are not on dialysis due to the complexities of injectable treatments, resulting in an unacceptable risk of red blood cell transfusion.

There is also a need for alternative treatment options for dialysis patients who respond inadequately to ESAs and those on home dialysis. Patients with anemia of CKD would benefit from having the choice of an oral treatment option that can be continued throughout their entire clinical course.

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Roxadustat is a first-in-class oral therapy designed to consistently correct and maintain hemoglobin across the spectrum of patients with CKD anemia. Its novel mechanism of action is based on an oxygen-sensing pathway, a discovery that was awarded the 2019 Nobel Prize in physiology or medicine.

It's a small molecule inhibitor of
hypoxia-inducible factor prolyl hydroxylase, or
HIF-PH, the enzyme that regulates HIF activity.
HIF is responsible for coordinating a physiologic
response to decrease the oxygen levels. By
transiently inhibiting the enzyme, roxadustat
increases hemoglobin by mimicking the body's
natural response to low oxygen.

Now, let's take a closer look at its novel mechanism of action. Under normal oxygen conditions, HIF-PH enzymes hydroxylate the alfa subunit of HIF. This hydroxylation targets the HIF-alfa subunit for rapid degradation via the proteasome. When oxygen levels fall, HIF-PH enzymes become inactive and HIF-alfa degradation is

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This allows the formation of an active. prevented. HIF transcription factor, which leads to increased expression of HIF target genes, including those involved in erythropoiesis. This same pathway can be pharmacologically activated by roxadustat, which inhibits the HIF-PH enzymes. Roxadustat stimulates a coordinated erythropoietic response the same way the body naturally responds to low oxygen. This coordinated erythropoietic response is a key differentiator between roxadustat and currently available treatments for patients with CKD anemia. ensures sufficient iron availability for effective erythropoiesis to occur in the presence of physiologic levels of EPO. This is in contrast to ESAs that do not stimulate a coordinated erythropoietic response, and therefore lead to

We've worked closely with the FDA to design and adapt our phase 3 clinical development program.

At the end of the phase 2 meeting in 2012, FDA

supraphysiologic levels of EPO to increase red

blood cell production.

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requested that our program be powered to assess CV safety for the NDD and DD population separately as a result of CV safety concerns for ESAs, which we did.

Our first phase 3 study started shortly after that meeting and our pivotal phase 3 studies were completely enrolled in 2018. At our pre-NDA meeting in July of 2019, we reached agreement with the FDA on the final pooling strategy and the analytical methods to use for the evaluation of the ND and DD populations, respectively. We then submitted our NDA in December of 2019. Additionally, roxadustat is approved in China and Japan, and on June 24th, we received a positive opinion from the CHMP for the approval of roxadustat in the EU.

Now, let me share the clinical development program. We've conducted an extensive CKD clinical development program, which includes more than 13,000 patients. Nine phase 2 studies informed the sponsor in the development of the phase 3 program.

Since patients with CKD anemia who are

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dialysis-dependent and not dialysis-dependent are quite different populations, we've conducted several studies in each group. Three NDD studies have been pooled in agreement with the FDA. These include Studies 001, 060, and 608, and three studies in dialysis-dependent patients have been pooled in agreement with the FDA. These include Studies 002, 063, and 064. Additionally, we'll show supportive evidence from Study 610 that compared roxadustat to an active control in NDD patients.

Six phase 3 studies were sponsored by

Astellas Pharma and conducted in Japan, two in NDD

patients and four in DD patients. Two phase 3

studies were sponsored by our affiliate in China

and conducted in China, one in each population.

Data from Study 613 and safety data from these additional studies have been presented in the briefing book for your reference. Our presentation will focus mainly on the results from our six pivotal phase 3 studies that demonstrate the efficacy and safety of roxadustat.

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Today you will see that roxadustat's efficacy and safety, including CV safety, was consistently demonstrated across the spectrum of patients with CKD. This includes patients not on dialysis and those on dialysis, whether recently started or stable and independent of information inflammation and iron status.

Each of our six pivotal studies met its

primary efficacy endpoint of mean change from

baseline in hemoglobin. Roxadustat showed a

statistically significant and clinically meaningful
improvement versus placebo in the NDD trials and

was comparable to ESA in the DD trials.

Additionally, roxadustat demonstrated a reduction
in red blood cell transfusions.

The CV safety profile of roxadustat was comparable to placebo in NDD and epoetin alfa in DD and the general safety profile appears to be acceptable. The totality of the evidence supports the use of roxadustat to increase and maintain hemoglobin levels for patients with CKD anemia who need additional treatment options. Our proposed

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indication is for the treatment of anemia due to CKD in adult patients not on dialysis and on dialysis.

With that background, I'll take you through the agenda. Next, Roberto Pecoits will describe the significant unmet need in patients with CKD anemia; then Dr. Lynda Szczech will present the efficacy data from our clinical program; followed by Dr. Dustin Little, who will present roxadustat's safety profile. Finally, Dr. Steven Fishbane will give his clinical perspective and conclude our presentation.

All external experts have been compensated for their time. We also have experts from FibroGen and AstraZeneca with us to help address your questions. Thank you. I will now turn the presentation over to Dr. Pecoits.

Applicant Presentation - Roberto Pecoits-Filho

DR. PECOITS-FILHO: Good morning. I'm a practicing nephrologist caring for patients with anemia CKD for 20 years. My research focus has been to observe practice patterns across the

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spectrum of CKD, and I was an investigator in several of the recent CKD anemia trials. From this perspective, I'll highlight the limitations of current therapies and discuss the unmet medical need for patients with anemia CKD.

To understand and appreciate the unmet need, we must consider the CKD patient journey and how several factors influence our treatment decisions.

CKD progresses across stages as kidney function declines. When eGFR approaches 15 mL per minute, some patients and their nephrologists would opt for non-dialytic conservative management. The majority begins that transition to dialysis why a few prepare for a transplant, clearly the superior form of kidney replacement therapy.

Currently in the U.S., 88 percent of patients receive in-center hemodialysis, while 11 percent receive peritoneal dialysis, and 2 percent home hemodialysis. Utilization of home dialysis is quite low and transplants are infrequent. However, there's great interest from clinicians and patients in increasing their use,

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and current standard of care for anemia management presents limitations to achieve this.

With each advancing stage of CKD, the prevalence and severity of anemia increases. The dark blue bars represent the proportion of patients who are potentially in need for anemia treatment, with hemoglobin levels lower than 10 grams per deciliter. Note that one-third of stage 5 are candidates for treatment. Patient symptoms, which worsen as CKD progresses, are important drivers to begin anemia treatment.

Let me now briefly review the pathophysiology of anemia in CKD. In healthy individuals, as oxygen tension decreases in kidney and liver, the stabilization of hypoxia-inducible factor promotes the production of erythropoietin and induces the release of iron into the circulation. Epo stimulates the differentiation of stem cells in the bone marrow, and available iron is utilized in the synthesis of hemoglobin and maturation of red blood cells.

In an anemia CKD, this process is disrupted,

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but current treatment options have limited actions in this complex pathophysiology. While erythropoiesis stimulated agents, or ESAs, target step 4, iron supplementation targets step 5. HIF stabilization and its downstream consequences are simply not addressed.

Now let's review the current standards of care and its significant limitations. Our current treatment options are ESA, iron therapy, and for those not responding, blood transfusion, however, we lack therapeutic alternatives with mechanism of actions beyond just prescribing iron and ESAs.

These treatments are logistically complex, particularly in non-dialysis patients and home dialysis patients, leading to another treatment that contrasts with the evidence-based guideline recommendations.

For ESA treatment to be effective, patients must be iron replete and a separate physiological dose of intravenous iron can be required, risking vein viability for dialysis vascular access. The most challenging group of patients are those

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identified as hyporesponders since they do not achieve target levels of hemoglobin despite high doses of IV iron and ESAs.

The main objective of CKD anemia treatment is to avoid transfusions, yet this remains common across the spectrum of CKD. Transplantation, the therapy with best quality of life, survival, and rehab potential, can be compromised in transfused patients.

Let's discuss our history with anemia treatment and how it has impacted current standard of care. Following the introduction of ESA into clinical practice, the average hemoglobin level in U.S. patients rose because of an increase in the doses of the ESAs. Landmark studies demonstrated an increase in cardiovascular risk related to ESA treatment and led to an FDA boxed warning in 2007 and label update in 2011. The result was lower ESA doses and hemoglobin level declines.

Since this time, the decision of when and how to best treat anemia in CKD is based on guidelines developed by more than 10 organizations,

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including the global KDIGO, which recommends 1 treatment of anemia in both dialysis and 2 non-dialysis CKD patients to increase hemoglobin to 3 a revised target of 9 to 11.5 grams per deciliter. 4 The consensus of this evidence-based guideline is 5 that the objective of treatment should be to 6 improve patient's quality of life and to reduce the 7 risk of red blood cell transfusions. 8 The cost of achieving the recommended 9 hemoglobin level with last ESA has been an 10 increasing IV iron therapy and supraphysiological 11 12 ferritin levels. Although a goal of treatment is to avoid transfusions, they are still common in 13 14 both non-dialysis and dialysis patients. This figure shows data in older patients not 15 on dialysis. First, know that 39 percent of those 16 patients are not treated at all. We also see not 17 18 only a 40 percent infusion rate but that 19 transfusions are the most common treatment of anemia in this population. 20 21 Transfusion also remains common in the dialysis population, and in 2018, 23 percent of 22

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patients on dialysis received at least one 1 transfusion. The scenario becomes consequential 2 when we appreciate the impact of transfusions in 3 CKD, especially in those considering a transplant. 4 When I see patients with advanced CKD, the 5 most impactful thing I can do is to help them get a 6 kidney transplant. Transfusion results in 7 clinically significant increases in antibody 8 9 production, with a negative impact in transplant outcomes. 10 First, an increase in the panel reactive 11 antibodies, or PRAs, commonly associated with 12 transfusions delays the perspective of patients 13 receiving a kidney transplant. Unfortunately, many 14 transfused patients will never be transplanted 15 since mortality rates are very high in dialysis 16 patients on the wait list. 17 18 Also, as you can see in this graph, 19 sensitized patients are also at high risk of rejection when they receive a kidney transplant. 20 21 failing transplant has catastrophic events from a

patient's perspective, sending many dialysis

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patients back to dialysis every year. Highly sensitized patients also represent a burden to the healthcare system, as they require more complex and costly induction and immunosuppressive treatments.

The final unmet need in CKD anemia treatment is that many patients do not properly respond to current therapies. The ESA hyporesponsive patients are often inflamed and show signs of functional iron deficiency. They represent an important challenge to effective management, typically requiring high doses of iron and ESAs. ESA hyporesponsive patients have higher transfusion mortality and hospitalization rates and increase health care costs compared to patients who have an adequate response to ESA therapy.

In summary, my options to care for patients with CKD anemia, or CKD, are clearly insufficient, and sometimes non-existent. Physicians and patients would benefit from an oral therapy for anemia that promotes endogenous erythropoiesis, improves iron utilization, and offers a choice for ESA hyporesponders.

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The logistical changes in the non-dialysis setting have compromised iron and ESA delivery due to the time and distance of therapies, caregiver demands, and disease burden that directly contributes to the high transfusion rates currently observed. We need a treatment that addresses the challenges of delivering iron through the intravenous route and in high doses; one that optimizes home treatments and enables continuous therapy across a transition from the non-dialysis to the dialysis stages of disease treatment. Finally, we need a therapy that improves access to transplant by lowering the risk of transfusions. Thank you for your time and consideration. I will now turn the presentation over to Dr. Szczech. Applicant Presentation - Lynda Szczech DR. SZCZECH: Thank you, and good morning. I am Linda Szczech, vice president of clinical development and medical affairs at FibroGen, and a nephrologist. I am pleased to be here today to present our clinical results showing that

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roxadustat increases hemoglobin in patients with chronic kidney disease and anemia. I will also present data that demonstrate the efficacy of roxadustat independent of baseline iron status or inflammatory state.

We've conducted an extensive clinical development program in chronic kidney disease.

I'll focus my presentation on the results from our six pivotal phase 3 studies, three in patients who are not on dialysis and three in patients who were on dialysis.

The prespecified primary efficacy endpoints were met in each individual study. To facilitate the presentation, I'll present the pooled results, as the results of the individual studies were similar in direction and magnitude. Remember, individual studies were controlled for multiplicity and this was not employed in the pooled analysis.

I'll begin with Study 001, 060, and 608 that enrolled NDD patients. These three trials were similarly designed as global, randomized, double-blind, placebo-controlled studies. Eligible

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patients had baseline hemoglobin levels of less than 10 grams per deciliter. Two of the studies were randomized 2 to 1 roxadustat to placebo and the third was randomized 1 to 1. Treatment durations ranged from 1 to 4 years.

The primary endpoint across all three pivotal NDD studies was the mean change from baseline in hemoglobin averaged over weeks 28 to 52 regardless of rescue therapy. Several secondary and non-hemoglobin related endpoints supported the primary analysis. Today, I will focus on the clinically meaningful endpoints listed here. Other secondary endpoints can be found in your briefing document.

More than 4,000 patients were enrolled in the three pivotal NDD studies, nearly 2400 to roxadustat and 1900 to placebo. Eighty-three percent of roxadustat-treated patients and 71 percent of placebo-treated patients have data to allow the assessment of the primary efficacy endpoint. Information on the proportion of patients completing treatment with full follow-up

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on safety will be presented later during the safety presentation.

At baseline, patients were similar between groups and representative of NDD patients globally. The majority were white followed by Asian. In the U.S., 32 percent of enrolled patients were black or African-American. Our NDD study population had an advanced stage of CKD.

Overall, the median eGFR was about

17 milliliters per minute, with 20 percent of
patients having a baseline eGFR of less than 10.

This is noteworthy for two reasons. First, most
prior phase 3 studies of marketed anemia products
for this population excluded patients with baseline
values of less than 15; and second, the median eGFR
for patients at the time of dialysis initiation in
the U.S., according to the 2020 USRDS annual data
report, was 9.2 milliliters per minute.

Additionally, the mean CRP was greater than
7. For context, the mean CRP in the general
population, as reported by the U.S. NHANES study,
was 0.02. Finally, roughly 40 percent of patients

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were iron deplete at baseline.

Now let's turn to the primary efficacy endpoint results. In the individual trials, roxadustat met the prespecified primary endpoint. Patients treated with roxadustat experienced statistically and clinically significant improvements in mean hemoglobin regardless of rescue therapy compared to placebo.

This graph shows the change in hemoglobin over 52 weeks with a treatment difference of 1.7 grams per deciliter favoring roxadustat. We will present further results on changes to the treatment algorithm and its effect on the shape of this curve later in the presentation.

This forest plot illustrates the placebo-adjusted treatment effect for roxadustat within the individual studies. The treatment effect for each of these studies was statistically significant compared to the placebo. This significant treatment effect favored roxadustat over a wide range of subgroups.

You'll notice a clear trend that those with

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the lowest baseline eGFR had the greatest change in hemoglobin from baseline. This is because patients with the lowest eGFR at baseline also had the lowest hemoglobin levels at baseline. Importantly, we saw that irrespective of baseline iron repletion status, patients on roxadustat have the same significant hemoglobin response. The comparable efficacy between roxadustat-treated patients who were iron replete, and those who are iron deplete, was observed without differences in roxadustat doses or a greater need for rescue therapy with IV iron or transfusion. Significantly fewer roxadustat-treated patients required rescue therapy or red cell transfusion compared with placebo-treated patients. Rescue therapy, on the left, included both red cell transfusion, ESA use, or IV iron. Of importance, only 2 percent of patients in the roxadustat arm received IV iron in the first 52 weeks. Shown on the right, roxadustat treatment also reduced the incidence of transfusions compared

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to placebo. Considering the importance of transfusion avoidance that Dr. Pecoits discussed as an unmet need, roxadustat decreased the risk of patients requiring transfusion by 74 percent.

Finally, with respect to the NDD pooled trial, I will highlight the ability of roxadustat to treat anemia during the dialysis initiation period. Please note that patients enrolled in the NDD studies continued treatment, even if their underlying kidney disease required them to start dialysis.

Here we show hemoglobin levels for NDD patients who are receiving roxadustat when they transitioned to dialysis during the study. In this graph, time zero is dialysis initiation. It shows hemoglobin levels in the few months before and after the transition from NDD to begin dialysis. Roxadustat provided stable hemoglobin levels during this very challenging time in a patient's life.

Overall, roxadustat consistently corrected and maintained hemoglobin in NDD patients with anemia CKD. Statistically significant treatment

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differences favored roxadustat compared to placebo. 1 Hemoglobin was increased regardless of baseline 2 iron replication status and clinically meaningful 3 reductions in red cell transfusions were achieved. 4 Next, I'll present our three pivotal phase 3 5 studies in dialysis-dependent patients, 6 Studies 001, 063, and 064. These were randomized, 7 open-label trials. The FDA requested we pool these 8 studies because roxadustat was compared to a single 9 comparator, epoetin alfa. Please note that these 10 studies included ESA-naïve patients and those 11 converted to roxadustat from ESA treatment. 12 The primary endpoint was similar to the NDD 13 14 trials. Mean change from baseline in hemoglobin averaged over weeks 28 to 52 regardless of rescue 15 The secondary endpoints focused on therapy. 16 hemoglobin change based on inflammatory status 17 18 because of the historical underperformance of 19 epoetin alfa in patients who are inflamed. I'11 focus on the endpoints listed here. 20 21 We randomized almost 4,000 patients to roxadustat or epoetin alfa; 79.4 percent of the 22

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roxadustat and 85.1 percent of the epoetin alfa group have data to allow the assessment of the primary endpoint. Baseline demographics and characteristics were similar between the groups and representative of the patients who require dialysis globally. Eighteen percent of patients identified as black globally. Among U.S. patients, 39 percent were African American.

The mean CRP at baseline was similar between the groups and elevated in the same manner as seen in patients with NDD. Of note, serum ferritin levels were approximately 600 in the global cohort. This is roughly twice that of normal, which is usually 100 to 300.

Elevated ferritin levels are common in U.S. dialysis patients. The DOPPS Clinical Practice

Monitor of August 2020 reported that the mean ferritin level in the U.S. was greater than 800.

These markedly elevated levels of ferritin in the DD population suggest impaired iron utilization, also called functional iron deficiency. We will discuss this in detail later.

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Now let's look at the results. In the pooled DD analysis, roxadustat was comparable to epoetin alfa in the mean change in hemoglobin from baseline averaged over weeks 28 to 52. This graph shows the change in hemoglobin with a treatment difference of 0.26 grams per deciliter favoring roxadustat.

Please recall that the DD population comprised patients whose anemia was being corrected in patients who were converting from ESA to roxadustat. This is reflected in the absolute change in hemoglobin from baseline. Based on the hemoglobin change, roxadustat met its primary endpoint of noninferiority across all DD studies. The treatment effect favored roxadustat compared to epoetin alfa.

Based on phase 2 data that showed that roxadustat-treated patients have the same hemoglobin response and maintenance of iron stores, whether they were treated with oral or IV iron, we evaluated the mean monthly IV iron use in our phase 3 program.

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In the phase 3 studies, oral iron was encouraged and IV iron supplementation was permitted if the patient had an inadequate response to oral iron or couldn't tolerate it, and the patient was iron deficient, as determined by a ferritin of less than 100 or a TSAT of less than 20.

Shown here is the mean monthly IV iron use from week 1 through the first year on treatment.

The endpoint compared IV iron use between weeks 28 to 52, and during that period, roxadustat-treated patients required less monthly IV iron use than patients receiving epoetin alfa.

Additionally, fewer patients in the roxadustat group required red cell transfusion compared to the epoetin alfa group. These results demonstrate that roxadustat is at least as efficacious as epoetin alfa and are clinically meaningful to our patients.

Finally, I will review the results from approximately 400 peritoneal dialysis patients who participated in the global trials. As compared to

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epoetin alfa, roxadustat provided a similar treatment difference among patients on peritoneal dialysis in the primary endpoint of change from baseline in hemoglobin. Additionally, as shown on the right graph, patients who received roxadustat required fewer red cell transfusions during the treatment period than those who received epoetin alfa. Next, I'll further discuss roxadustat efficacy in patients with inflammation. The effect of inflammation on erythropoiesis and anemia treatment is complicated. It is important to emphasize that hepcidin is a key negative regulator of iron homeostasis that increases with inflammation and results in iron sequestration or trapping, which can conceptually be referred to as functional iron deficiency. In patients receiving dialysis, this inflammation as subsequent iron trapping leads to increased IV iron use to attempt to overcome the

functional iron deficiency and results in even

higher ferritin levels. Therefore, inflammation,

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whether measured by elevated CRP or hepcidin, causes unique problems in the treatment of anemia of CKD.

I will now present data demonstrating how roxadustat mobilizes iron and benefits patients on dialysis. Hyporesponsiveness, as mentioned by Dr. Pecoits, is an important problem with ESA therapy mediated through inflammation and lack of iron availability to the bone marrow. CRP as a marker of inflammation is elevated among patients who are less responsive to ESAs due to inflammation.

While there is no single or standard definition of hyporesponsiveness, arguably, many definitions are population-specific, examining patients who are less responsive than the rest of the population. Therefore, it may be clinically relevant to look at the spectrum of responsiveness within a population to best understand the relationships with treatment.

To explore the efficacy of roxadustat across the spectrum of inflammation, we first evaluated

levels of baseline CRP.

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hemoglobin response relative to baseline levels of CRP collected in 4 of the 6 pivotal trials. As we look at increasing baseline quintiles of CRP from left to right, roxadustat treatment results in an equally robust increase in hemoglobin compared with epoetin alfa.

It is important to examine the dosing requirements now to complete this picture. Here, we see an important difference in dosing between the two treatments. In yellow, epoetin alfa-treated patients required progressively higher doses to maintain hemoglobin response at higher

The weekly doses of epoetin alfa rose from 112, among patients with the lowest degree of inflammation, to 139 units per kilogram in patients with the highest degree, a 24 percent increase.

Conversely, roxadustat dosing requirements, in blue, did not increase at higher levels of CRP.

Next, we explored how a reduction in hepcidin may affect the sequestration of iron seen in inflammation and functional iron deficiency and

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may be of a more direct benefit to patients. 1 will begin with a broad overview of how roxadustat 2 affects iron stores consistent in both NDD and DD 3 patients, and we'll look at NDD patients first. 4 Hepcidin, on the right, is significantly 5 decreased with roxadustat treatment and is 6 associated with increased serum iron levels and 7 decreased ferritin. Please note that this increase 8 in serum iron occurred with roxadustat therapy 9 concurrent with less IV iron use -- only 2 percent 10 received IV iron in the first 52 weeks -- and even 11 those significant amounts of endogenous iron were 12 being used to produce hemoglobin. 13 While the fact that one marker of iron 14 stores is increasing, serum iron, while another 15 marker is decreasing, ferritin, may seem to be a 16 paradox, the most important thing to remember here 17 18 is that ferritin is a marker of intracellular iron 19 stores. The decline in ferritin in roxadustat-treated patients as compared to 20 21 placebo-treated patients is consistent with a reduction in hepcidin that leads to the 22

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mobilization of trapped intracellular iron stores and their subsequent delivery to the bone marrow.

The iron results in the DD population were similar and provide us the opportunity to compare roxadustat to epoetin alfa. In the DD trials, roxadustat increased serum iron in patients while allowing for less IV iron administration, lower transfusion rates, and slightly higher hemoglobin levels. Conversely, serum iron decreased in patients who received epoetin alfa.

Although hepcidin and ferritin were reduced in both treatment arms, the greatest reduction occurred in the roxadustat-treated patients. As in the NDD-treated patients, the increased iron and decreased ferritin with roxadustat treatment suggest an increased iron mobilization from previously trapped stores. This represents a unique physiologic difference between roxadustat and epoetin alfa. Now let's look at how it's clinically relevant to patient outcomes.

A high serum ferritin or hepcidin level could be a marker of inflammation or iron

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sequestration, which contribute to hyporesponsiveness to ESA treatment. We therefore examined the efficacy of roxadustat, on the right, and epoetin alfa, on the left, according to baseline quintiles of these values, and serum ferritin is presented in this slide. As a reminder, the normal range for ferritin is roughly 100 to 300. The mean serum ferritin at baseline was approximately 600, almost twice that of normal, with the highest quintile, 20 percent of the treatment arm, having values higher than 1000. In a clinical setting, high ferritin values often lead to significant doses of IV iron to attempt to overcome the inflammation-induced functional iron deficiency so that hemoglobin can be effectively produced.

Among patients treated with epoetin alfa, on the left, those with the highest ferritin levels, in red and orange, had the lowest hemoglobin levels. This lower hemoglobin response occurred despite patients receiving higher epoetin alfa doses. The mean difference between quintiles,

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between the red and orange, and the other three quintiles was as high as 0.5 grams per deciliter at some points. In contrast, roxadustat-treated patients, on the right, had similar increases in hemoglobin across all baseline ferritin quintiles.

To explore the clinical relevance of these observations, I will discuss the differences in transfusion rate between roxadustat-treated and epoetin alfa-treated patients, focusing on the subset of patients with functional iron deficiency due to inflammation identified here.

In this exploratory analysis of patients based on baseline ferritin levels, roxadustat-treated patients received transfusions less frequently than epoetin alfa-treated patients in all quintiles. In the epoetin alfa arm, in yellow, when comparing the highest quintile of ferritin, on the right, to the lower four quintiles combined, on the left, the incidence of transfusion is highest in the highest quintile of ferritin, likely reflective of the lower hemoglobins achieved in this highest quintile, relative to the rest of

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the epoetin alfa arm.

In short, epoetin alfa-treated patients had the highest baseline serum ferritin levels,

20 percent of the cohort; so in those patients they had both the lowest hemoglobin levels and the highest rate of transfusion in both treatment arms.

The same relationship of underperformance of epoetin alfa is seen when hemoglobin levels are compared among quintiles of hepcidin, also potentially reflective of a group with functional iron deficiency, and these analyses are described in the briefing book.

In summary, the DD clinical trials show that roxadustat was comparable to epoetin alfa regardless of baseline inflammation.

Roxadustat-treated patients achieved clinically meaningful reductions in red cell transfusions and IV iron use, particularly in patients with markers of iron stores suggesting functional iron deficiency. Overall, the roxadustat clinical program provided consistent efficacy. Roxadustat increased hemoglobin and managed anemia across the

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continuum of CKD. 1 Thank you. I'll now turn the presentation 2 over to Dr. Little, who will present the safety of 3 roxadustat. 4 Applicant Presentation - Dustin Little 5 DR. LITTLE: Thank you, Dr. Szczech. 6 I'm Dustin Little. I'm a nephrologist, and 7 I'm the roxadustat global clinical head at 8 AstraZeneca, and I'll be presenting the safety 9 results from our clinical program. 10 Today, I will be discussing the pooled 11 cardiovascular safety results for our pivotal 12 phase 3 program, a review of specific events from 13 14 the program, and a summary of our risk management plan. Let's start with some history of how the 15 roxadustat program came to be. 16 The program was initially intended to 17 18 consist of pivotal efficacy trials without a pooled 19 assessment of cardiovascular safety. Based on FDA feedback to study cardiovascular safety, a 20 21 meta-analysis of pivotal phase 3 trials was planned, and Studies 001 and 002 were added to the

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program.

Key endpoints include MACE, or major adverse cardiovascular events, and MACE-Plus. MACE consisted of all-cause mortality, myocardial infarction, and stroke, and MACE-Plus is defined as MACE plus hospitalization for heart failure or hospitalization for unstable angina. The use of all-cause mortality in the cardiovascular safety composites is consistent with precedent from prior CKD anemia cardiovascular trials and was suggested by FDA.

The aim of our program was to generate a sufficient safety database to assess the cardiovascular safety of roxadustat compared to placebo in non-dialysis-dependent CKD and compared to epoetin alfa in dialysis-dependent CKD. The roxadustat program is the largest phase 3 CKD anemia program ever conducted. In the placebo-controlled NDD population, we studied 4,270 patients, 830 of whom had a major adverse cardiovascular event during the study. Due to the placebo-controlled design, we observed differences

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in treatment discontinuation, which I will tell you more about on the subsequent slides.

In the epoetin alfa-controlled DD program, we studied 3,880 patients, 645 of whom had a major adverse cardiovascular event during the treatment period. In the DD population, treatment discontinuation was more balanced by treatment group compared to NDD.

Reported cardiovascular events were sent to a blinded central independent event review committee for adjudication, and the program is monitored by an independent data monitoring committee. The size of the program allowed for the use of a noninferiority margin of 1.3 based on precedence and an FDA guidance on the evaluation of cardiovascular safety for new drugs, which was active at the time of the design of the roxadustat program.

Let's first focus on cardiovascular safety in the NDD population. As shown earlier, baseline characteristics were well balanced between treatment groups. More roxadustat patients

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completed treatment compared to placebo patients at 62 percent and 40 percent, respectively. result of this, the mean treatment duration for roxadustat patients was 1.6 years compared to 1.2 years for placebo. Where possible, patients were followed for cardiovascular events after treatment discontinuation, and 88 percent of roxadustat and 85 percent of placebo-treated patients were assessed for MACE through the end of the study. Vital status, whether a patient is alive or dead, could be confirmed via public record search at the end of the study for some patients, and 91 percent of patients in both treatment groups had complete follow-up for all-cause mortality.

Before we discuss the results of the cardiovascular safety analyses of the program, I'd like to take a few slides to discuss the impact of these differences in treatment discontinuation.

This curve shows the proportion of patients remaining on treatment over time by treatment group. As you can see, the maximum treatment

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duration was more than 3 years.

Large differences in treatment
discontinuation were noted early in the study. For
example, 20 percent of placebo patients
discontinued treatment in the first approximately
4 months following randomization compared to nearly
9 months for roxadustat. This pattern was also
noted in time to discontinuation of treatment in
50 percent of patients by treatment group, which
occurred approximately 6 months later in the
roxadustat group.

As a result of these differences in treatment discontinuation, roxadustat-treated patients had substantially more exposure to study treatment compared to placebo patients. To investigate whether the types of patients who stopped treatment are different for the two treatment groups, which would lead to bias in on-treatment analyses, we evaluated the characteristics of patients remaining on roxadustat over time compared to placebo.

This figure shows the median baseline

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estimated glomerular filtration rate at different time points following randomization for patients remaining on roxadustat and placebo treatment.

Median eGFR was balanced at baseline, however, because patients with more severe CKD tend to have more severe anemia, placebo patients with lower baseline eGFR were more likely to require anemia rescue therapy and stop treatment compared to placebo patients with less severe CKD.

As a result of this, the population of patients remaining on placebo progressively became a population of patients with less severe baseline CKD. By contrast, roxadustat patients' anemia was effectively managed, resulting in patients with more advanced CKD being able to continue with longterm treatment.

This curve shows the proportion of patients remaining on treatment following dialysis initiation by treatment group. When including patients who started dialysis after treatment discontinuation, a similar proportion of patients required dialysis initiation overall. However,

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more patients started dialysis while on roxadustat treatment because placebo patients who were close to dialysis were more likely to stop placebo treatment due to low hemoglobin values and requirement for treatment of anemia; and because most dialysis patients require anemia treatment, placebo patients discontinued study drug at very high rates following dialysis initiation.

Due to these differences in treatment discontinuation, both prior to and following dialysis initiation, more patients starting dialysis were able to continue roxadustat therapy.

This slide shows the percentage of dialysis patients among patients remaining on treatment over time. For example, at 12 months following randomization, approximately 20 percent of patients remaining on roxadustat have started chronic dialysis compared to approximately 10 percent of placebo patients, and the magnitude of this difference increased over time. This is clinically important because patients starting dialysis have substantially higher risk of cardiovascular events

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and other events compared to non-dialysis patients. 1 Although this complicates the interpretation 2 of NDD CV safety data, it is important to note that 3 we have a dedicated analysis of the cardiovascular 4 safety of roxadustat compared to epoetin alfa in 5 over 1,500 incident or new-to-dialysis patients, 6 7 which I will present later. This slide shows mortality rates by NDD CKD 8 stage and by month following dialysis initiation in 9 U.S. patients. As you can see, mortality risk 10 increases as NDD CKD becomes more severe and 11 12 increases markedly with dialysis initiation. On the prior slides, I've shown you that 13 14 patients with more severe CKD and those requiring dialysis initiation were overrepresented in the 15 roxadustat group over time due to differences in 16 treatment discontinuation. Because these patients 17 18 have higher cardiovascular risk, this means that 19 the balanced CV risk that was present at baseline due to randomization was not preserved among 20 21 patients remaining on treatment. Thus, 22 on-treatment analyses will be heavily biased

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against roxadustat.

So with that background, let's discuss how we can analyze the roxadustat NDD cardiovascular safety data. The ideal analysis would ensure that the effect of randomization in terms of equal risk by treatment group is preserved. This is not the case for on-treatment analyses due to differences in treatment discontinuation.

In an ideal analysis, missing data and time off treatment should be minimized and there should be an adequate number of patients with events. ITT or on-study analyses include all events which occur following randomization, including those which occur after treatment discontinuation.

This has the advantage of balancing patient risk throughout the analysis period. However, in the roxadustat program, ITT on-study analyses have some missing data, with more missing data in the placebo group, and they include a substantial proportion of time off treatment, particularly among placebo patients.

In the roxadustat NDD program, no single

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analysis achieves all of these objectives in an ideal manner. However, different analyses have different strengths and weaknesses and can be used collectively to assess the cardiovascular safety of roxadustat.

This slide shows several analyses which have been performed comparing MACE risk for roxadustat to placebo. I'd like to point out that the hazard ratio and 95 percent confidence intervals cross 1 for all of the analyses except for the on-treatment analysis.

We've already discussed how the on-treatment analysis is profoundly affected by differences in treatment discontinuation and how the ITT on-study analysis is limited by greater missing data and greater time on treatment in the placebo group.

Overall, analyses which preserve the benefit of ITT analysis in terms of equal risk by treatment group, but which minimize the impact of missing data and greater time off treatment in the placebo group, have hazard ratio point estimates of close to 1.0, supporting that risk for MACE is comparable

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for roxadustat compared to placebo.

These analyses include ITT on-study analyses of patients with baseline eGFR of greater than or equal to 10 milliliters per minute, which excludes the quintile of patients with the lowest baseline eGFR who were most affected by differential treatment discontinuation.

We also performed ITT on-study analysis with censoring at dialysis initiation in order to focus on the cardiovascular safety of roxadustat in non-dialysis patients, and we also performed ITT on-study analysis with censoring at one year following randomization because that is a time frame at which differences in treatment discontinuation were of a lower magnitude.

Additionally, the hazard ratio point estimate for the 992 patients from the United States who were more representative of U.S. non-dialysis patients was 0.99.

In contrast to the NDD placebo-controlled data, Study 610 is an active comparator NDD study not affected by large differences in treatment

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discontinuation. The MACE hazard ratio point estimate for roxadustat compared to darbepoetin alfa was 0.81. These results are supportive of the cardiovascular safety of roxadustat in non-dialysis patients.

Coming back to the placebo-controlled NDD program, here are the Kaplan-Meier curves from MACE risk over time for roxadustat compared to placebo.

On the left is the overall ITT or on-study analysis, and on the right is the analysis with censoring at dialysis initiation.

The latter analysis is, as mentioned previously, performed in order to focus on roxadustat's cardiovascular safety in non-dialysis patients and is less affected by missing data and greater time on treatment in the placebo group. In both figures, the curves track closely together, consistent with comparable MACE risk for roxadustat and placebo.

This figure shows the results of MACE-Plus cardiovascular mortality and each of the components of MACE-Plus. For each event, two results are

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shown, overall NDD, which is on top, and NDD with censoring at dialysis initiation, which is also known as NDD-NDD. For each event, the 95 percent confidence interval crossed 1.0.

Let's turn now to the DD population. As shown earlier, baseline characteristics were well balanced between the treatment groups. Fifty-eight percent of roxadustat compared to 66 percent of epoetin alfa patients completed treatment.

When interpreting these data regarding the proportion of patients completing treatment, it is important to remember that these were event-driven studies with a maximum treatment duration of more than three years. A similar proportion of patients were followed for MACE events through the end of the study and a similar proportion of patients in both treatment groups had complete follow-up for all-cause mortality.

As mentioned previously, the DD population included patients untreated with ESA at baseline as well as patients on ESA treatment prior to enrollment. As described earlier and consistent

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with nephrology convention, incident dialysis
patients were predefined as patients who were
randomized to roxadustat or epoetin alfa within
4 months following dialysis initiation. Incident
dialysis patients were generally not on anemia
treatment at baseline or had been recently
initiated on treatment prior to enrollment.

In contrast to the incident dialysis
subgroup, stable or prevalent dialysis patients
were mostly on long-term ESA treatment at baseline.
Thus, patients randomized to roxadustat required
conversion to a different mechanism of anemia
treatment, whereas ESAs patients continued ESA.

Following completion of study treatment, roxadustat patients would be expected to convert to ESA particularly within the first 4 weeks following the conclusion of treatment, whereas ESA patients would be expected to continue treatment with ESA.

Here are the results of the on-treatment plus 7-days analysis set for the pooled DD assessment of MACE for roxadustat compared to epoetin alfa. This analysis window was the

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agreed-upon primary analysis set with FDA. The analysis shows similar cardiovascular risk for roxadustat compared to epoetin alfa, with a hazard ratio point estimate of 1.02 and 95 percent confidence interval upper bound of 1.20.

Results in the predefined subgroup of incident dialysis are shown. The incident- or new-to-dialysis population is considered to be particularly relevant for three reasons.

First, anemia treatment is often initiated during the incident dialysis period. Second, incident or new-to-dialysis patients are exposed to substantial cardiovascular risk, and it was important for us to ensure that we had no cardiovascular safety signal in this traditionally high-risk population.

And third, patients starting dialysis in our NDD program were those who were most substantially affected by differences in treatment discontinuation; so analysis of the incident dialysis subgroup of the overall dialysis population is required to fully understand

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roxadustat's cardiovascular safety in patients recently initiated on dialysis.

Results in the stable dialysis subgroup of patients who were randomized to either continue ESA or convert to roxadustat are also shown. Finally, the on-treatment plus 28-days analysis set is shown as a support of analysis. Overall, the results are consistent with comparable risk for MACE for roxadustat and epoetin alfa.

Here's the Kaplan-Meier curve for MACE for the DD population. The curve tracked closely together consistent with similar MACE risk for roxadustat and epoetin alfa. The hazard ratio for MACE-Plus for roxadustat compared to epoetin alfa was 0.91. Looking at each component of MACE-Plus, risk was similar for roxadustat and epoetin alfa.

Study 613 was an outlier in the DD program and was not pooled with the pivotal DD studies because of its unique design with two ESA comparators. It was a study of exclusively stable dialysis patients and contained no incident dialysis patients. Patients' short-acting ESA at

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baseline were randomized to either roxadustat or epoetin alfa, whereas patients on long-acting ESA were randomized to either roxadustat or darbepoetin alfa. All patients were from Europe, with 79 percent from Eastern or Central Europe. another difference between 613 and the pivotal DD trials is that starting roxadustat doses were higher in Study 613. Study 613 was not powered for the assessment of cardiovascular safety, therefore it is instructive to consider the impact of adding Study 613 to the DD pool. Although 613 was an outlier in terms of the design and the cardiovascular safety results, when pooled with the pivotal dialysis studies, the overall conclusion of comparable MACE risk for roxadustat and epoetin alfa is unchanged, as the hazard ratio point estimate was 1.08 with 95 percent confidence interval upper bound of 1.24. Before I summarize the cardiovascular safety data in the roxadustat program, I'd like to point

higher targets.

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out that in our program, we did not compare roxadustat to ESA dose according to the trials that demonstrated increased cardiovascular risk, but rather dosed according to current labels, which have been updated to minimize cardiovascular risk.

As you know, the normal hematocrit in CHOIR trials compared ESA dose to two different hemoglobin targets and increased cardiovascular events were noted in the groups randomized to the

Importantly, the hemoglobin targets used in patients treated with ESA in the roxadustat program were more consistent with the control groups in normal hematocrit in CHOIR, and it is in this setting that we had MACE, MACE-Plus, and all-cause mortality hazard ratios ranging from 0.91 to 1.02 in the DD pool and of less than 1 in Study 610.

In conclusion, roxadustat's cardiovascular safety has been evaluated across the continuum of patients with CKD anemia. In the non-dialysis-dependent population, the risk of MACE was comparable to placebo and there was no

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increased cardiovascular risk noted for roxadustat compared to darbepoetin alfa in the 610 trial, which was not affected by substantial differences in treatment discontinuation.

In the overall DD population, patients receiving roxadustat had comparable risk of MACE compared with the epoetin alfa, and similarly in the incident- or new-to-dialysis and the stable dialysis subgroups, MACE risk was comparable between the treatment groups.

Next, I'll review data on the following safety topics where imbalances were noted: seizures, infections, vascular access thrombosis, and deep vein thrombosis.

Labels for approved ESAs warned about seizures, which have been observed with ESA therapy. We performed a standard metric query for convulsions to capture all adverse events potentially referring to seizures. We noted that more roxadustat patients had seizure events versus the comparators. Although the number of patients with a reported baseline history of seizure was low

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in the roxadustat program, these patients disproportionally contributed to the imbalance, and we consider that patients with a history of seizure should be treated with roxadustat with caution.

Patients with severe CKD are at high risk for infection, and infection is among the leading causes of death in dialysis patients. In the NDD program, patients at highest risk for infection were more likely to discontinue placebo compared to roxadustat; therefore, differences in treatment discontinuation likely contributed to the observed imbalances in serious and fatal infection compared to placebo, particularly in on-treatment analysis as is shown here.

By contrast, in the DD program where treatment discontinuation was more balanced, the incidence of serious and fatal infection was similar between treatment groups.

This table shows all infection serious adverse events in the NDD population with an incidence of at least 1 percent in either treatment group. These adverse events are consistent with

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the most common events expected in a population of patients with severe chronic kidney disease. As may be expected, considering the differences in treatment discontinuation described previously, the incidence of these infections were higher in the roxadustat group. By contrast, the incidence of the most common infection SAEs in the DD program were generally similar for roxadustat and epoetin alfa.

To summarize our infection data, we saw imbalances in serious and fatal infection in the placebo-controlled NDD program but not the active control DD program. Because ESAs aren't known to cause serious or fatal infections in CKD anemia, these results suggest that the results in the NDD program may be related to bias due to differential treatment discontinuation.

ESAs have been observed to increase thrombosis risk, particularly when treating to higher hemoglobin targets. What is reported here is an overall composite of thrombosis events, which include vascular access thrombosis, venous events

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such as deep vein thrombosis, and arterial events such as myocardial infarction. In the NDD and DD populations, the types of thrombosis reported were typical of those observed in the CKD population with no imbalances observed in rare or atypical thrombotic events.

Overall, the rates of potential arterial thrombosis events were similar between roxadustat and comparator as demonstrated by the results of adjudicated myocardial infarction and stroke.

However, for both the NDD and DD populations, there were more vascular access thrombosis and deep vein thrombosis events in roxadustat-treated patients.

Weights of deep vein thrombosis pulmonary embolism were higher for roxadustat compared to placebo in non-dialysis patients. In the DD program, the incidence of pulmonary embolism, or PE, and the overall incidence of DVT and PE was similar for roxadustat compared to epoetin alfa. However, the incidence of DVT was higher at 1.5 percent for roxadustat compared to 1 percent for epoetin alfa.

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Vascular access thrombosis is a known risk of treatment of CKD anemia. Here, the term "vascular access thrombosis," or VAT, refers to thrombosis of an arteriovenous fistula or arteriovenous graft that is used, or planned to be used, for hemodialysis vascular access. Potential vascular access thrombosis events were centrally adjudicated by a committee which was blinded to treatment assignment, and the incidence of adjudicated VAT is what is shown here.

VAT events occurred more frequently in roxadustat-treated patients in the NDD and DD populations. The DD data is the focus of our VAT evaluation because NDD patients would not be expected to have dialysis access at baseline and because NDD patients requiring dialysis access were those who were most affected by differential treatment discontinuation. Among dialysis patients overall, VAT was noted in 13 percent of roxadustat compared to 10.5 percent of epoetin alfa patients.

Part of our investigation of our thrombosis data included an evaluation of the rates of

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thrombosis over time. We found that rates of thrombosis and VAT with roxadustat were highest during the initial treatment period and decreased over time, and the differences in rates for roxadustat compared to epoetin alfa were also highest during the early treatment period.

This corresponds with the time frame when differences in mean hemoglobin values were largest for roxadustat compared to epoetin alfa and when rapid rates of hemoglobin rise were most common for patients treated with roxadustat.

This figure shows rates of thrombosis and vascular access thrombosis by hemoglobin rate of rise using analytic methods agreed to between FDA and the sponsor. In both roxadustat- and epoetin alfa-treated patients, higher rates of thrombosis were observed at higher rates of rise of hemoglobin.

Notably, rapid rate of rise of hemoglobin was observed more frequently with roxadustat treatment. These results, taken together with the results on the previous slide, support that

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thrombosis and vascular access thrombosis risks are associated with rapid rate of hemoglobin rise with roxadustat treatment.

We also evaluated the possibility of a relationship between dose and thrombosis risk, and noted that rates of thrombosis and VAT appeared to be higher at higher doses of roxadustat. Although these data have limitations and do not conclusively demonstrate that higher roxadustat doses are causative of thrombosis, we considered whether roxadustat doses could be lowered by targeting a lower hemoglobin value.

But before we discuss roxadustat dosing, I'd like to review the results of these analyses in NDD patients. In NDD patients, rates of thrombosis AEs were higher at higher rates of hemoglobin rise. We also noted in NDD that rates of thrombosis tended to be higher at higher roxadustat doses.

In light of these findings, we are proposing changes to roxadustat dosing to mitigate thrombosis risk. First, we plan to lower the hemoglobin target from 10.5 to 12 grams per deciliter to 10 to

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11 grams per deciliter. As I will show you, this allows for us to use lower roxadustat doses throughout the treatment period and it also allows us to minimize hemoglobin overshoots with roxadustat treatment. Additionally, we plan to lower roxadustat starting doses both in ESA untreated and ESA conversion patients. In subsequent slides, I will show you the expected impact of these changes on the incidence of rapid hemoglobin rise.

Finally, we recommend that patients who are unresponsive to roxadustat receive no more than three consecutive increases in roxadustat dose. As above, based on the results from our clinical program, we discussed with FDA to target hemoglobin values of 10 to 11 grams per deciliter, and we knew that lowering starting doses would lower the rate of hemoglobin rise and the incidence of early hemoglobin overshoots.

We used modeling and simulation to help us decide which specific starting doses to propose and to evaluate the expected impact on roxadustat

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dosing of the proposed lower hemoglobin target. To assess the reliability of our simulations, we compared simulated mean hemoglobin values using the phase 3 roxadustat doses to the actual phase 3 hemoglobin values in the clinical program, and as you can see here, the simulation results closely matched the observed clinical results.

The left figure on this slide shows the simulated incidence of rapid rate of hemoglobin rise with the phase 3 doses compared to the proposed lower starting doses. As you can see, the change in starting dose is anticipated to reduce the incidence of rapid rate of hemoglobin rise quite substantially, which is expected to lower risk of thrombosis and specifically vascular access thrombosis.

The figure on the right half of the slide shows simulated mean hemoglobin values over time with the phase 3 compared to the proposed dosing.

As you can see, the proposed dosing is expected to lead to mean hemoglobin values which increase into the target range, with less potential for

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hemoglobin overshoots, particularly during the initial treatment period.

This slide shows similar simulation results for patients converted from ESA. Again, the incidence of rapid rate of hemoglobin rise is substantially lower and mean hemoglobin values are more stable during the initial treatment period with the proposed dosing changes.

This slide shows the simulated mean roxadustat doses with the lower starting doses and the lower hemoglobin target. Overall, this strategy is expected to reduce roxadustat doses by more than 25 percent during the treatment period.

Here, I'm showing you, once again, the incidence of thrombosis by roxadustat dose. Using the phase 3 starting doses and phase 3 target hemoglobin, the average roxadustat dose would be expected to be approximately 3 milligrams per kilogram per week, a dose above which higher rates of thromboses were observed.

By contrast, mean doses using the proposed starting dose and the proposed hemoglobin target

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are expected to be 2.2 milligrams per kilogram per week, which corresponds with doses at which lower thrombosis rates were observed.

Here is the same analysis for DD patients. As you can see, the proposed updated dosing is expected to reduce roxadustat doses by more than 30 percent. This slide shows rates of thrombosis and VAT by roxadustat dose in the DD population.

Once again, predicted mean dose using the phase 3 dosing corresponds with doses that are close to ranges where increased rates of thromboses were noted, whereas predicted mean dose using the proposed dosing corresponds with doses at which observed thrombosis rates were lower.

In terms of risk management, in addition to the changes to dosing, we plan to communicate all important safety information and recommendations for risk mitigation associated with the use of roxadustat in the prescribing information for healthcare providers and a medication guide for patients, and we also plan to communicate risks and educational materials for healthcare providers. We

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additionally plan to utilize product labeling to mitigate risk.

In addition to the proposed dosing changes, we will also make recommendations on the appropriate frequency of hemoglobin monitoring and to consider withholding treatment for severe or life-threatening thrombosis and to manage all thromboses promptly.

We consider that patients with a history of seizure should be treated with roxadustat with caution and that patients should promptly report symptoms, new onset seizures, or increase in seizure frequency to their healthcare provider. We also recommend to avoid starting roxadustat in patients with an active severe or serious infection, that patients be monitored for signs and symptoms of infection, and that any infection be promptly treated.

On the slide after this, I will review with you a proposal for a postmarketing study to confirm that vascular access thrombosis risks are similar for roxadustat and ESA with the proposed roxadustat

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dosing regimen, but first, I'd like to point out that the practice model for U.S. dialysis patients is uniquely suited to prospectively evaluate the effectiveness of our risk minimization strategies for lowering VAT risk in the postmarketing setting using real-world evidence.

First of all, there are more than 500,000 prevalent U.S. dialysis patients with more than 100,000 patients starting dialysis each year. This large pool of patients allows us to effectively match patients treated with the standard of care to patients treated with roxadustat.

Additionally, anemia treatment data is collected systematically with hemoglobin values assessed monthly as part of typical clinical practice. Patients dialysis accesses are assessed for the presence of thrombosis in conjunction with every dialysis session and it is noted when patients require new dialysis access following a thrombosis event.

Finally, by studying patients treated with roxadustat in the real world, we can assess a

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broader more generalizable patient population, and we would expect the results to be directly translatable to clinical practice. So with this in mind, we're proposing a post-approval, prospective, matched cohort study of U.S. dialysis patients treated with roxadustat compared to ESA.

Both ESA untreated and conversion patients will be studied. Patients will be treated according to approve labels, and roxadustat-treated patients will be compared to matched ESA-treated patients based on predefined criteria.

The main objectives will be to compare VAT risk for roxadustat and ESA and to assess risk factors for VAT with both treatments. We plan to study 5,000 roxadustat-treated patients compared to 5,000 ESA-treated patients with one year of observation time per patient. With this sample size, we expect approximately 1,000 events, which is expected to allow us to estimate the incidence rate of vascular access thrombosis in each treatment group plus or minus 1 event per 100 patient-years.

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In conclusion, our large database allowed for a comprehensive evaluation of the roxadustat safety profile. We observed comparable cardiovascular risk for roxadustat versus placebo and versus ESA in non-dialysis patients compared to ESA in dialysis patients. Patients treated with roxadustat had an increased incidence of vascular access thrombosis, deep vein thrombosis, and seizures, and we saw a higher incidence of fatal infections versus placebo in NDD patients, but not compared to ESA in DD patients.

We are proposing several strategies to manage these risks. First, product labeling will communicate warnings and precautions to physicians and a medication guide will communicate these risks to patients.

We're also proposing changes to dosing that will decrease the risk of thrombosis with roxadustat treatment, and we're proposing a postmarketing, real-world study of 10,000 patients to confirm that risk of VAT is similar for roxadustat and ESA with the proposed changes to

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roxadustat dosing. We will continuously evaluate, communicate, and mitigate risks, and we are committed to working with the FDA to further characterize the roxadustat safety profile in the post-approval setting.

Thank you, and I'll now turn the presentation to Dr. Fishbane.

Applicant Presentation - Steven Fishbane

DR. FISHBANE: Good morning. My name is

Steven Fishbane. I'm a practicing nephrologist and
a professor of medicine of the Donald and Barbara

Zucker School of Medicine at Hofstra/Northwell and
chief of nephrology for the Northwell health
system. I've taken care of patients with kidney
disease and have studied this condition for more
than 25 years. I'm an active member of the KDIGO
global anemia and kidney disease guideline group.

From this vantage point, I'd like to share my perspective on the use of roxadustat for patients with the anemia of CKD. The history here is important. Treatment of anemia is critical in the care of patients with CKD. Forty years ago,

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before ESA therapy was available, hemoglobin levels in patients receiving dialysis were severely depressed. For these patients, life was truly miserable and many were unable to function or even perform basic activities of living.

Blood transfusions were the standard of care. There were many problems associated with repeated blood transfusions in addition to cost, patient inconvenience, and infections; but more importantly, the development of antibodies that make it difficult to get a kidney transplant and also iron overload, which was almost universal, frequently requiring chelation treatment.

The approval of ESAs in 1989 was an important advance for patients, but there's not been much innovation in anemia treatment since the first ESA approval. I believe roxadustat now represents an important advance.

Despite the breakthrough that ESAs were in dialysis anemia, problems in dialysis anemia treatment remain today in 2021. The first problem relates to patients who are transitioning from CKD

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to begin dialysis. These first few months on dialysis are very difficult with sharply increased hospitalizations and mortality risk. Previously untreated anemia greatly complicates this incident dialysis period with rapid hemoglobin fluxes and high ESA doses.

On the left, the first figure from DOPPS shows what current anemia treatment looks like at the start of dialysis. You can see how low hemoglobin levels are, and it takes months to reach a stable hemoglobin concentration.

The second figure on the right is what

Dr. Szczech showed earlier, how roxadustat allows

for a more orderly hemoglobin transition to

dialysis. I have long waited to be able to treat

my office CKD patients for this issue with an oral

agent like roxadustat that would create this kind

of smooth transition to dialysis.

A second issue, once patients are on dialysis, ESA hyporesponsiveness is a frequent concern. A poor ESA hemoglobin response leads to transfusions, high ESA doses, and an associated

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increased risk of cardiovascular events. Iron deficiency and inflammation are widely accepted as the major causes of hyporesponsiveness. Both complicate current ESA treatment leading to very high IV iron doses and unresolved anemia of inflammation. Roxadustat meaningfully addresses both of these leading causes of hyporesponsiveness.

We saw from the data how roxadustat improved iron availability and reduced IV iron doses in the figure on the left; and as for inflammation, how it worked well despite elevated CRP without the need for the high doses, as was true for epoetin alfa on the right.

The third issue has to do with home dialysis. The country right now is making a major push to increase home dialysis, but both injected ESA therapy and intravenous iron complicate this effort. In the figure, we saw data Dr. Szczech showed on how remarkably well roxadustat worked in patients on home dialysis PD. It's clear to me that roxadustat can help with each of these current dialysis anemia problems.

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Now, for patients with kidney disease not yet on dialysis, anemia management is currently even more challenging. We made strides in dialysis anemia treatment, but non-dialysis patients have truly been left behind. Up to 50 percent of these patients have anemia, yet most are untreated.

The reason is largely because of the complexities and logistical issues associated with both injected ESAs and intravenous iron and the frequent clinic visits that are required. In fact, data show that less than 15 percent of non-dialysis patients receive ESA therapy, and although two-thirds of non-dialysis patients have iron deficiency, very few receive iron treatment.

As a result, in the U.S. today, if non-dialysis patients are treated for anemia at all, it is likely with a blood transfusion. More patients receive blood transfusions than either ESAs or intravenous iron.

Now this is important. Forty percent of patients receive a blood transfusion in the two years prior to starting dialysis. Transfusions are

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highly relevant, as they cause antibody production, and this makes it harder to receive a kidney transplant, clearly the best treatment for ESRD, and for those that receive a transplant, the risk of rejection is increased. These 10 studies show that as a result of blood transfusions alloantibodies frequently develop. With each study, the left-sided black horizontal bar shows that after transfusion,

sensitization averages 20 to 40 percent. In the white bars, the non-transfused patients, antibody

production is far less. 12

> More recent data shows that red cell transfusions result in clinically significant increases in HLA antibody strength and breadth, and these HLA antibodies, crucial for transplantation, turn out to be directly related to the specifically donated blood.

If an oral drug like roxadustat was available, the treatment of anemia in non-dialysis CKD, which is so limited today by complexity and inconvenience, would be much more readily

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accomplished with the potential, as we saw in these phase 3 studies of a 74 percent reduction in blood transfusions, and that could result in far fewer issues with antibody production that delay, complicate, and prevent kidney transplantation.

It is because of the complexity and logistical issues that nephrologists uncommonly

logistical issues that nephrologists uncommonly treat non-dialysis anemia, but the need is absolutely there, and that need is supported by the recommendations of global guideline groups. In fact, there are many anemia in kidney disease guideline groups throughout the world. These expert panels have examined the totality of risk and benefit data.

There is a widespread unanimous consensus
that supports anemia treatment in both dialysis and
non-dialysis CKD. They speak to improving symptoms
and raising hemoglobin to reduce blood
transfusions. Similarly, anemia treatment of both
dialysis and non-dialysis CKD are also widely
approved by FDA and other international regulatory
agencies. The FDA labels say ESAs are indicated

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for the treatment of anemia for CKD in patients on dialysis and patients not on dialysis.

Now, obviously the purpose of today's meeting is not to determine the need for anemia treatment; the world's expert guideline groups have spoken very clearly on the subject. There is no controversy; rather, it's to determine the risk and benefit balance of this drug roxadustat.

It's my strong belief that the benefits of treating anemia with roxadustat in dialysis and non-dialysis CKD patients clearly outweigh the risks, and this novel oral therapy addresses the anemia needs of the spectrum of CKD patient populations, providing therapeutic options and specific benefits as compared and contrasted to the present standard of care.

I'd like to note that I've carefully reviewed the sponsor's plan to adjust recommended roxadustat dosing to limit hemoglobin rate of rise to mitigate thrombosis risk. Importantly, the relationship of ESA dosing, hemoglobin, and thrombosis risk has long been known and is part of

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the label for all marketed ESAs. The clear 1 demonstration in this program of the relationship 2 between hemoglobin rate of rise with thrombosis 3 points to this long known and well understood 4 phenomenon, and the sponsor's new dosing plan 5 should be highly effective for reducing risk. 6 There are a few disease states that have 7 only one type of treatment available. 8 Nephrologists and patients would like to have choice to be able to decide which treatment is most 10 appropriate. For a patient doing well on ESAs, 11 12 there may be no reason to change, but for my patients, I certainly would like to have choice. 13 In conclusion, we saw that in dialysis there 14 remains unmet needs that oral roxadustat could 15 readily address. I'd like to repeat one in 16 particular. The major effort in the U.S. right now 17 18 to increase transplantation and home dialysis, 19 roxadustat is uniquely situated to help with both. The reduction in transfusions would improve 20 21 transplantation access and the oral route would 22 ease the path to home dialysis.

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In non-dialysis CKD, roxadustat would greatly improve the lives of many patients by making anemia treatment so much easier and thereby greatly reducing the number of transfusions and improving opportunities for transplantation. Thank you. I'd now like to turn the presentation over to Dr. Eisner.

DR. EISNER: Thank you, Dr. Fishbane.

My name is Mark Eisner, and I am the chief medical officer at FibroGen. At this time, we'd be happy to take your questions.

Clarifying Questions

DR. LEWIS: We will now take clarifying questions for FibroGen. Please use the raised-hand icon to indicate that you have a question and remember to put your hand down after you've asked your question. When acknowledged, please remember to state your name for the record before you speak and direct your question to a specific presenter, if you can.

If you wish for a specific slide to be displayed, please let us know the slide number, if

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possible. Finally, it would be helpful to acknowledge the end of your question with a thank you and the end of your follow-up question with "That is all for my questions," so we can move on to the next panel member. I am going to begin the guestions. two questions. One, Dr. Szczech, you have spent a considerable amount of time talking about reducing iron dose. I think on slide CO-45, it was from 52 to 66 in the two groups, reducing roxadustat dose in inflamed patients and reducing transfusion. However, disturbingly, despite those hypothetical advantages, if anything, there was an increased safety signal or certainly not a noninferior. Can you associate any of those things, for example, the lower iron dose, with any outcome that would be clinically meaningful to a patient -- and I will give you a moment to look at that -- or even less transfusions with more transplants? The other question is that the average dialysis patient is on 13 unique home meds, one of

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which is a phosphate binder which interferes with roxadustat absorption. This is a heavy burden for them to keep track of, and it is very difficult to do medication reconciliation. It is not dissimilar in the CKD-5 population. No compliance data was presented.

I wonder if you have compliance data. I also can't figure out if the patients on dialysis

also can't figure out if the patients on dialysis actually got the pill at dialysis or somewhere else, or took it at home -- but certainly in the non-dialysis population you should have compliance data from people taking it at home -- and if there were any associations of lack of compliance with either not hitting the hemoglobin targets or rapid rises in hemoglobin.

Thank you. Those are my two questions, and I'll wait for your answers.

DR. EISNER: EISNER: Thank you. It's Mark Eisner. Thank you for the questions. I'll ask Dr. Szczech to address your first question about iron.

Dr. Szczech?

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DR. SZCZECH: Thank you very much. 1 I don't have a slide for this, however, 2 we did pursue differences in MACE based on 3 differences in changes in ferritin, ferritin at 4 baseline, and there did not appear to be any 5 differences in the major adverse cardiovascular 6 outcomes or any other important safety signals, 7 based on ferritin levels at baseline or changes in 8 ferritin levels at baseline. 9 10 I'll pause here to see if that answers your question. 11 12 DR. LEWIS: Thank you. That answers my question. 13 14 DR. SZCZECH: Thank you. The second question --15 DR. EISNER: Go ahead, Dr. Szczech, please. 16 DR. SZCZECH: The second question was about 17 18 transfusion and differences in transplant outcome. 19 May I ask you to clarify that so I can give you the appropriate information? 20 21 DR. LEWIS: Sure. And actually you could have picked any one of them; I don't know that you 22

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have to go through all of them. So if less 1 transfusions, the big advantage is more 2 transplants, did you see more transplants in the 3 roxadustat group? 4 DR. SZCZECH: Thank you very much for that 5 Transplantation, as everyone knows, is 6 highly dependent on multiple factors, which 7 includes your region. The average waiting time for 8 a kidney unfortunately in the U.S. can be as much as four to five years in some areas. 10 So a reduction in transfusion benefits a 11 patient not only initially during their NDD period 12 but for years to come after dialysis is initiated. 13 14 They get on the transplant --DR. LEWIS: Dr. Szczech, I'm sorry. 15 interrupt you? Do you have data to show that your 16 roxadustat group got more transfusions? 17 18 understand the theoretical benefit. 19 DR. SZCZECH: I was trying to explain that examination of this particular endpoint would have 20 21 been out of scope for these studies because, of course, they only looked at the NDD period. So no, 22

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we do not have data, and I was just explaining why. 1 Thank you for focusing me. 2 DR. EISNER: Then there was a question, 3 Dr. Szczech, about the compliance both in the NDD 4 and the DD setting. Can you please address that 5 question? 6 7 DR. SZCZECH: I would be happy to. Linda Szczech. 8 9 So it is important to know that roxadustat is not dialyzable, so it can be given both on 10 dialysis and off dialysis. For patients who are 11 dialysis-dependent, you mentioned the interaction 12 with phosphate binders, and we did not demonstrate 13 14 a significant issue in patients who were either on phosphate binders or were not on phosphate binders 15 in our phase 2 studies. Because this is a 16 titratable drug, if the bioavailability is 17 18 decreased by the phosphate binder, the drug can be 19 titrated up to the hemoglobin that is required. I show you here that the interactions with 20 21 the phosphate binders are more so associated with the sevelamer and the calcium-containing phosphate 22

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binders. No interaction was seen with lanthanum, 1 and that's a minor technical point that I just 2 wanted to share. 3 In terms of compliance, we found excellent 4 compliance in our clinical trials, and I can try to 5 get you some information after the break to break 6 down exactly how well patients were able to comply 7 with their therapies using the TIW regimen. 8 Did the dialysis patients 9 DR. LEWIS: receive the drug in the dialysis unit? 10 DR. EISNER: Dr. Szczech, the question's for 11 you, please. 12 DR. SZCZECH: Thank you. Linda Szczech. 13 14 We did not specify that they needed to receive the drug in the dialysis unit, but based on 15 our knowledge, we believe that many of them did. 16 DR. LEWIS: Thank you. That's the end of my 17 18 questions. 19 Our first question is Dr. Packer. DR. PACKER: Thank you so much. I just 20 21 wanted to ask just one general question and then one specific one. The general question is the 22

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mechanism of action. 1 This drug inhibits prolyl hydroxylase, but 2 there are at least four isoforms of that enzyme, 3 and they interact with different isoforms, 4 hypoxia-inducible factor alfa. 5 Can you tell us which isoforms of prolyl 6 hydroxylase are inhibited by roxadustat and what 7 HIF isoforms are potentiated? 8 DR. EISNER: Yes. Thanks for your question. 9 I'll ask Dr. Walkinshaw to address it for you. 10 Dr. Walkinshaw? 11 DR. WALKINSHAW: Yes. Hello. Gail 12 Walkinshaw here. Roxadustat actually inhibits all 13 three of the major isoforms of the prolyl 14 hydroxylase enzyme, so PHD1, PHD2, PHD3. 15 There is a fourth enzyme which you refer to 16 which is a transmembrane prolyl hydroxylase. 17 18 haven't studied that specifically to know whether roxadustat inhibits that, and the function of that 19 enzyme and its role in HIF stabilization is very 20 21 unclear. In terms of the stabilization of HIF, roxadustat stabilizes both HIF-1 alfa and HIF-2 22

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alfa. 1 DR. PACKER: Just to follow up on that, 2 HIF-1 alfa and HIF-2 alfa often have diametrically 3 opposite effects on tissues. And in particular 4 with respect to the heart, HIF-1 alfa is 5 proangiogenic, proinflammatory, and profibrotic. 6 HIF-2 alfa has the opposing effects. 7 So when you inhibit prolyl hydroxylase, 8 depending on which enzyme your inhibiting, which 9 enzyme is already activated and the tissue, you 10 might have a greater potentiation of HIF-1 alfa 11 12 compared with HIF-2 alfa. Would that be fair? 13 14 DR. EISNER: Dr. Walkinshaw, I'll ask you to respond. 15 DR. WALKINSHAW: Yes. Gail Walkinshaw here. 16 Yes, I think you bring up a very good point. 17 18 It's one of the big challenges that we have in 19 interpreting the literature because many people study either HIF-1 alfa or HIF-2 alfa using genetic 20 21 tools, and that never really gives us an insight into what we would expect with roxadustat where 22

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we're stabilizing both of those HIF-alfa paralogs. 1 Also, a lot of the published reports use the 2 genetic tools which leads to chronic captivation of 3 HIF-1 alfa or HIF-2 alfa, and that's, again, not 4 what we're doing with roxadustat. We're only 5 transiently stabilizing both of those. So really, 6 that's why we rely heavily on our non-clinical 7 toxicology studies because that's, really, the only 8 way we can understand what to expect if we're just 9 transiently stabilizing HIF-1 alfa and HIF-2 alfa. 10 DR. PACKER: The only reason I bring this up 11 is because HIF-1 alfa, we really would not want to 12 produce sustained increases in HIF-1 alfa. And the 13 14 effects of prolonged activation of HIF-1 alfa could have many adverse affects biologically and 15 pathophysiologically, which are independent of the 16 rate of rise of hemoglobin. 17 18 That's why I asked the question because, 19 you're right, the available basic science literature, it's really hard to make this 20 21 prediction. But I make it only because of my second question, which is to segue to the endpoint 22

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I think I would like to personally focus on, which 1 is all-cause mortality. 2 The reason for focusing on that is, gee, 3 all-cause mortality is really important and, two, 4 all-cause mortality is fairly agnostic about 5 mechanisms. So if HIF-1 alfa potentiation leads to 6 proinflammatory and profibrotic effects, you may 7 not pick that up on a conventional MACE endpoint. 8 So just focusing on all-cause mortality, you 9 have a lot of all-cause deaths in your trials, so 10 you have a good event rate and the ability to 11 discern what's going on. And I agree with you that 12 your NDD populations, the analyses are really 13 difficult. 14 It's really very, very complicated to try to 15 tease out the event rate, but you don't have that 16 problem in the DD population. In fact, your 17 18 retention rate in the DD population is a little bit 19 higher in the epo group than the roxa group. Can you put up a slide on all-cause 20 21 mortality in the four individual trials in the DD population? 22

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DR. EISNER: Yes, we will do that.
                                                  I will
1
      ask Dr. Little to respond to that question.
2
     while we're bringing it up, I'd like to ask Dr. del
3
     Balzo to just briefly talk to you about our
4
     preclinical data on cardiovascular issues.
5
             Dr. del Balzo, can you summarize that for
6
     us? And then I'll to Dr. Little on the all-cause
7
     mortality aspect of your question. Yes, Victor
8
     does also here. Yes, thank you for the question.
9
             DR. DEL BALZO: Yes. Ughetta del Balzo
10
             Yes, thank you for the question.
11
12
             I think it's important to just take a moment
      to look at our toxicology program at a high level.
13
14
      In this program, we have evaluated roxadustat
      chronically up to one year in monkeys. In general,
15
      as observed with ESA, the high roxadustat doses
16
      induced alterations caused by exaggerated
17
18
     pharmacology. So these are consequences of
19
      increased red blood cell production inducing
     polycythemia and hemoconcentration.
20
21
             [Inaudible - audio gap].
             DR. PACKER: Hello?
22
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DR. EISNER: Dr. del Balzo, I think we lost 1 Why don't we go to Dr. Little for the 2 vou. clinical data in DD for all-cause mortality. 3 Dr. Little? 4 DR. LITTLE: Dustin little here. 5 Dr. Packer, I have a slide that has the 6 7 pooled all-cause mortality result and then the results for each of the three pivotal trials, and 8 9 then we can bring up the slide that showed the results for 613. 10 The pooled hazard ratio point estimate was 11 1.02, and you see the hazard ratio point estimates 12 for each of the three pivotal studies. Overall, we 13 14 didn't see a significant interaction and we saw a substantial overlap between the confidence 15 intervals. 16 Now I have the slide that also shows 17 18 Study 613. When we add Study 613 to the pool, 19 Dr. Packer, we mentioned that that study is an outlier in terms of the all-cause mortality 20 21 results. We have a hazard ratio point estimate of 1.11; but again, overall in the three pivotal study 22

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pools, a hazard ratio point estimate of 1.02.
1
     we consider that there's no increased risk of
2
      all-cause mortality with roxadustat compared to
3
      epoetin alfa.
4
             DR. PACKER: Well, let me have you pause
5
     there for a moment, and let me just make sure that
6
      I totally understand how you're going about doing
7
     this.
8
9
             This is all-cause mortality --
             DR. LEWIS: Dr. Packer?
10
             DR. PACKER: Yes?
11
                          I'm sorry. We have a lot of
             DR. LEWIS:
12
      questions.
                 Can you keep this a little bit shorter?
13
14
             DR. PACKER:
                           Okay.
             Can you explain why your analysis of
15
     all-cause mortality differs from that of the FDA?
16
             DR. EISNER: Dr. Little, I'll ask you to
17
18
      respond to the question, please?
19
             DR. LITTLE: Dustin Little.
             Dr. Packer, I may need to ask for
20
21
      clarification for the analysis of all-cause
     mortality on differing. What we have here are the
22
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results for our pooled Cox regressions.
1
             DR. PACKER: Julia, I'm going to pause
2
3
     here --
             DR. LEWIS: Yes, thank you.
4
             DR. PACKER: -- but I just want to make the
5
     point that the analysis that they just showed is
6
     based on 264 plus 277 events. The FDA analysis of
7
     all-cause mortality in the same population has more
8
      than 800 events.
9
10
             DR. LEWIS: Okay. Thank you, Dr. Packer.
             I'm going to go on to Dr. Bairey Merz.
11
     please, everybody, remember, even though I'm
12
      announcing you, to state your name for the record
13
14
     before you ask your question.
             DR. BAIREY MERZ: Thank you, Dr. Lewis.
15
             Noel Bairey Merz. This is a question for
16
     Dr. Fishbane, two just very general questions.
17
18
             You said in your remarks that likely
19
     dialysis patients on epo probably would not be
      encouraged to change to the oral roxa, and as a
20
21
     guideline writer and as a representative of what
      likely will be future guidelines, what do you think
22
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the guidelines will say about who would prefer to be on the oral form? And as a second related question, would you advise for or against non-nephrology prescribing this medication? Thank you.

DR. FISHBANE: Yes. Thank you for the question. In dialysis, I'm not going to anticipate, we are going to be having a KDIGO updated global guideline group that will be coming out. But in terms of the use of the drug in patients on dialysis, what I said before my presentation was that if I have a patient who is currently on ESA, and is doing well, and is not experiencing problems, then I wouldn't necessarily see a reason to change that patient.

On the other hand, look, I'm the chief medical officer for a 15-dialysis unit chain, and in individual dialysis units there are maybe units where we prefer not to be using our nurses running around opening up vials of medications, filling syringes, and injecting patients. There may be places where we prefer three times a week doing

oral treatment. 1 Certainly, with issues related to 2 hyporesponse, with issues related to home dialysis, 3 4 and this very difficult problem we have with the transition in those first very difficult months of 5 dialysis, I see a really important opportunity in 6 terms of oral treatment. But I think I'm not going 7 to go further towards anticipating what we'll do 8 with quidelines, but I do appreciate the question. 9 DR. LEWIS: Dr. Fishbane, we have quite a 10 few more questions. Could you address Dr. Bairey 11 Merz's second question; would you recommend 12 non-nephrologists use this drug? 13 DR. FISHBANE: Yes, I generally recommend 14 that it would be best used in the hands of 15 nephrologists who are taking care of patients, 16 both --17 18 DR. LEWIS: Thank you. 19 DR. FISHBANE: Thanks. DR. BAIREY MERZ: Thank you. 20 21 DR. LEWIS: Thank you. Dr. O'Connor? And please announce yourself. 22

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DR. O'CONNOR: Yes. Chris O'Connor. This 1 is a question for Dr. Szczech or Dr. Little. 2 Ιn heart-failure trials, quality of life and 3 hospitalizations are very important outcomes. 4 Ιn page 28 and page 56 of your briefing document, in 5 28 you provide a quality-of-life analysis of the 6 SF-36. Although you got a statistically 7 significant difference despite getting an important 8 anemia correction, there were no clinically 9 meaningful differences. 10 Is it your position that this drug does not 11 improve quality of life despite correcting anemia? 12 That's part A. And part B is, what is the effect 13 of this drug on total and cardiovascular 14 hospitalizations? I saw the heart failure and 15 16 unstable angina trended in the right direction, but I didn't see total and cardiovascular 17 18 hospitalizations. 19 DR. EISNER: Yes. This is Mark Eisner. I'll ask Dr. Fishbane to address your question on 20 21 quality of life, and then Dr. Little on hospitalization. 22

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Dr. Fishbane?

DR. FISHBANE: Yes. Thank you.

Look, quality of life has been a historically very difficult challenge with respect to anemia treatment. A lot's been written on the subject. We could get into some of the issues if we want to discuss that further, but I do find that what we've seen here to be, despite the challenges, actually guite encouraging.

The key parameters in a double-blinded population with lots of patients here; we saw that for physical function of vitality, and that's where the keys have been in previous studies, a similar benefit, as we've seen previously, which gives us a sense that there is an opportunity here.

So we've got to be conservative with quality of life because of the difficulties of these studies, but I think despite the crude scales and mixed comorbidity, we're definitely seeing here an opportunity from that data to be able to do some of the guideline-recommended individualization of treatment. Thank you.

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DR. EISNER:
                           Thanks.
1
             Dr. Little, can you address the
2
     hospitalization question?
3
4
             DR. LITTLE: Dustin Little.
             Dr. O'Connor, I don't have a slide available
5
      for overall cardiac hospitalization, but I'd like
6
      to bring up adjudicated heart-failure
7
     hospitalization Kaplan-Meier plots for the pooled
8
     NDD and the pooled DD and just demonstrate those.
9
              You can see that for the pooled NDD
10
      adjudicated heart failure, hospitalization was
11
      somewhat numerically lower for roxadustat,
12
      especially earlier on, and then you see the hazard
13
      ratio point estimate of 0.83 with the upper bound
14
      of 1.05 for adjudicated heart failure
15
     hospitalization. In terms of overall
16
     hospitalization, 58.6 percent of roxadustat
17
     patients in the DD program required hospitalization
18
19
      compared to 59.5 percent of epoetin alfa patients.
              DR. LEWIS:
                          Thank you.
20
21
             Mr. Conway?
              (No response.)
22
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DR. LEWIS: Mr. Conway, you may need to unmute.

MR. CONWAY: Got it. Thank you very much; two quick questions, a general question to the presenters.

Because we're dealing with pooled data here, can you tell me whether or not any publications have been withdrawn based on initial publication?

And along that line, do you have -- please don't take this the wrong way, but I'm going to ask it.

Do you have full confidence in the data that was generated by your partner in China?

Then the second question actually I have for Dr. Fishbane is, given the data that you're looking at and given the population, or probably the expanse of the patient population that you were treating that you just identified across many facilities, would you approach African American patients differently with this medication who are on dialysis given the data?

I'm interested in that specifically because of outcomes. And by way of background, let me just

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say this. I was an ESA patient, iron infusion 1 patient, did it before dialysis, did it while I was 2 on home peritoneal dialysis, and I've had an 3 4 adverse incident. So I kind of have a general understanding of this in a little bit more detail, 5 but I'm interested in those two questions. 6 DR. EISNER: Thanks for your question. 7 It's Mark Eisner. In terms of your first question, 8 there were two parts. One was about do we have 9 full confidence in our trials in China, and we do. 10 This was conducted by FibroGen China, which is part 11 12 of FibroGen overall, so we have full confidence there. 13 14 I'll ask Dr. Szczech to address your question about publications. 15 DR. SZCZECH: Thank you very much. Linda 16 Szczech. We have had all of our publications 17 18 accepted and we're working on getting them into 19 publications. None of them have been withdrawn. DR. LEWIS: Thank you. 20 21 Dr. Parsa? DR. EISNER: And --22

DR. LEWIS: I'm sorry? 1 DR. EISNER: Pardon me for 2 interrupting -- it's Mark again -- but there was a 3 question about African American patients. Can we 4 have a moment to dress that? 5 DR. LEWIS: Surely. 6 DR. EISNER: Well, first just to say that 7 the efficacy in terms of hemoglobin was the same in 8 African American patients versus patients of other 9 races and ethnicities. 10 Let me ask Dr. Little just to briefly 11 address the safety in African American patients. 12 Dr. Little? 13 14 DR. LITTLE: Thank you. Dustin little. Mr. Conway, we did look at safety events by 15 race, and we didn't see -- let me bring up as an 16 example the MACE results in the dialysis-dependent 17 18 population. For black patients, we didn't see any 19 interaction by race. We consider that the overall safety results that we presented today are 20 21 applicable to black patients. I'd just like to briefly note that we're 22

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adding a 10,000-patient postmarketing study in the
1
      United States, and we would expect there to be a
2
      substantial number of African American patients in
3
      that study for us to look further at thrombosis,
4
      vascular access thrombosis overall and in
5
      African American patients.
6
                           I appreciate that. I just want
7
             MR. CONWAY:
      to make this note. The reason why I'm asking that
8
9
      question specifically is because I wanted to know
      what your data showed before you take it out and
10
      put it in the field, if that is the course that's
11
12
      taken, and expose patients to it. Thanks.
             DR. LEWIS:
                          Thank you.
13
             Dr. Parsa?
14
             DR. PARSA:
                          This is Afshin Parsa.
15
             Regarding this thrombosis risk on MACE and
16
     some of the subanalyses -- and the NDD certainly
17
18
     has been challenging, I appreciate the efforts -- I
19
     was wondering, were there any subgroup analyses
     looking at people on aspirin, clopidogrel,
20
21
     antiplatelet or anticoagulants, and whether that
22
     changes any of the outcomes?
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DR. EISNER: I'll ask Dr. Little to address 1 your question about whether antiplatelet agents 2 modify the safety of roxadustat. 3 Dr. Little? 4 DR. LITTLE: Dustin Little. We have 5 performed those analyses. I don't have a slide 6 7 available to show you that, but we did not observe any particular interaction in terms of 8 cardiovascular safety or thrombosis among patients 9 10 who were or were not on antiplatelet agents at baseline. 11 12 DR. LEWIS: Thank you. Dr. Thadhani, did that conclude your 13 14 question? If so, I'll move on to Dr. Wang. DR. WANG: Thanks a lot. Tommy Wang; two 15 quick questions. 16 One, I suspect a lot of the discussion is 17 18 going to focus on risk-benefit, and the point was 19 raised about risk-benefit in the dialysis patients with high CRP levels indicating inflammation as 20 21 potentially favoring roxadustat because of the less of the need for escalation of dosing. 22

Does the sponsor have any specific data 1 regarding either MACE events or adverse events in 2 3 roxadustat compared with epo in the high CRP patients in the dialysis population? That's one 4 question. 5 The second question, just returning to the 6 point Dr. Packer raised about VEGF, I appreciate 7 that there were relatively few malignancies that 8 9 occurred during the trials. Can the sponsor 10 comment on any general longer-term concerns regarding malignancies, either incident or 11 exacerbation or latent malignancy, and how they 12 plan to incorporate that into the postmarketing 13 trial that they've proposed, if postmarketing is 14 available? 15 DR. EISNER: Yes, thanks for your question. 16 I'll direct the first question on CRP in MACE to 17 18 Dr. Little. 19 DR. LITTLE: Dustin Little. Yes, Dr. Wang, we did perform an analysis of MACE risk by baseline 20 21 I'll bring it up momentarily, but as Dr. Szczech mentioned during her presentation, 22

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baseline CRP was actually only assessed in 4 of the 6 pivotal trials. It was not assessed at baseline in the two largest pivotal trials. In addition to the typical limitations of a subgroup analysis being post hoc and underpowered, we do have those limitations here.

In terms of the non dialysis population, we had 31 percent of patients without a CRP collected at baseline. When we look at the pattern of those events over time, we see absolutely no difference in MACE over the first approximately 12 months; so it's likely that differences in treatment discontinuation impacted these results.

Among the dialysis-dependent population, we had about 16 percent of patients without baseline CRP available, and interestingly among those patients, the hazard ratio point estimate was numerically favorable. I'm showing you the incident dialysis subpopulation because, simply, this is the group where we had less missing data, about 9 percent of patients, and we saw no interaction there.

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I'd like to briefly bring up the subgroup analysis by baseline ferritin tertiles because we know that ferritin is also elevated in inflammation and can be a marker of inflammation, and this was not so confounded by missing data. And in here we saw no interaction in NDD or DD. So we don't consider that there's an interaction by inflammation, and we consider that these ferritin values are more reliable due to the completeness of the data.

DR. EISNER: Then your second question about concern about malignancy, overall, when we look at our data overall, the short answer is we don't see an imbalance of malignancy, and we did follow patients up to four years. So to the best of our knowledge, we don't have a risk there.

In terms of the postmarketing setting, it's a good point. We are certainly in active discussions with FDA about the nature of the postmarketing real-world data study, and it certainly would be possible to add ascertainment of malignancy, benign or malignant tumors, to that

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1
      study. So it's a fair point, and thanks for
      raising it.
2
             DR. LEWIS: Dr. Thadhani, I apologize.
3
      skipped you. I'm going to let you have the last
4
     question.
5
             Those of you who have had your questions
6
     answered and don't have another one, please put
7
     your hands down, and we will make a list of the
8
     remaining people who have questions that we haven't
9
     got to, and hopefully we'll have time to work those
10
      in later.
11
             Dr. Thadhani?
12
             DR. THADHANI: Thank you, Dr. Lewis, and I
13
     will be brief.
14
             The sponsor nicely showed dose-response
15
      relationships, change in hemoglobin, and a proposal
16
      in a postmarketing fashion to potentially reduce
17
18
      the risk of thromboembolic events by the
19
     associative data. Certainly the adverse event
     profile includes other adverse events that were
20
21
      seen: infections, seizures, stroke, MI, acute
     kidney injury.
22
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Is there any evidence, even by way of 1 association, that changing or the proposals that 2 are suggested by the sponsor would have effects on 3 some of those other adverse events? Thank you. 4 DR. EISNER: No, thanks for the question. 5 That's a good question. I'll turn that to 6 Dr. Little to respond. 7 Dr. Little? 8 DR. LITTLE: Dustin Little. 9 Dr. Thadhani, when we looked through our 10 data, the clearest association that we saw was with 11 thrombosis events and that's what we're targeting 12 with our risk mitigation. We found some 13 publications that have demonstrated that similar 14 risk mitigation strategies appear to have decreased 15 thrombosis risk with ESAs. 16 When it comes to other events, like I said, 17 18 we did not see clear evidence that our mitigation 19 strategy would influence other events. Seizure, for example, has potentially been associated with 20 21 ESAs with more rapid increases in hemoglobin and treating to higher targets, and of course our 22

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mitigation strategy will lead to more gradual
1
      increases in hemoglobin and treating to lower
2
                But in sum, our risk mitigation is aimed
3
4
     at the thrombosis and vascular thrombosis risk that
     we noted in our clinical program.
5
              DR. LEWIS:
                          Thank you.
6
             We will now take a five-minute break.
7
                                                     Panel
     members, please remember that there should be no
8
      chatting or discussion of the meeting topic with
9
      anyone during the break. We will resume at 11:59.
10
      Thank you.
11
12
              (Whereupon, at 11:55 a.m., a recess was
13
     taken.)
              DR. LEWIS: Good afternoon. My name is
14
     Dr. Saleh Ayache. I'm a medical officer in the
15
     Division of Non-Malignant Hematology.
16
              DR. YU:
                      Dr. Ayache?
17
18
             DR. AYACHE:
                           I'm sorry.
19
             DR. YU: Can you give us one moment?
              Dr. Lewis, could you announce our return
20
21
      from the break?
              (Pause.)
22
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DR. YU: One moment, please. 1 Dr. Lewis, could you hear me? 2 I apologize. 3 DR. LEWIS: Thank you. 4 Actually, I don't think I muted myself there, but I want to ask all everybody to put their hands down. 5 Ms. Yu and I have made a list of the people 6 with remaining questions, and I think it will be 7 confusing if they stay up now. 8 We will now proceed with the FDA 9 presentation, Dr. Ayache. 10 (No response.) 11 DR. YU: Dr. Ayache, you might be on mute. 12 You may proceed 13 14 DR. AYACHE: Yes. DR. YU: Okay. Thanks. 15 FDA Presentation - Saleh Ayache 16 DR. AYACHE: Good afternoon. My name is 17 18 Dr. Saleh Ayache. I'm a medical officer in the 19 Division of Non-Malignant Hematology in the Office of Cardiology, Hematology, Endocrinology, and 20 21 Nephrology. I'll be presenting the FDA's major findings from the roxadustat application along with 22

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Dr. Jae Joon Song from the Division of 1 Biometrics VII, Office of Biostatistics. 2 Here is the review team assessing the 3 application. This is the outline of our 4 presentation. We will briefly discuss the product, 5 the regulatory history, and efficacy, but the focus 6 for our presentation will be the safety findings. 7 We will discuss the adverse events, major adverse 8 cardiovascular events, all-cause mortality, and 9 finally we will discuss some of the 10 interrelationships between thromboembolic events, 11 12 drug dose, hemoglobin, and rate of change of hemoglobin. 13 14 Roxadustat is a small molecule, oral, hypoxia-inducible factor prolyl hydroxylase 15 inhibitor that's posited to enhance erythropoiesis 16 by increasing endogenous erythropoietin and 17 18 reducing hepcidin. The drug is the first in its 19 The proposed indication is for the treatment of anemia due to CKD in adult patients 20 21 not on dialysis and on dialysis. Roxadustat is an orally administered tablet. 22

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The roxadustat dose is adjusted on the basis of the hemoglobin response. The drug is not approved in the U.S. It has been approved in China and Japan for patients on dialysis and not on dialysis.

Anemia is associated with increased cardiovascular morbidity and mortality. Anemia in patients with CKD is multifactorial, including erythropoietin deficiency, impaired ability to absorb and utilize iron, and blood loss and shortened RBC survival.

The current standard of care includes protein iron monitoring and supplementation of patients with iron deficiency. Most patients require ESAs to correct anemia and to reduce the need of RBC transfusion. However, transfusions have risks, including alloreactivity and increased risk of rejection after kidney transplantation.

ESAs are glycoproteins produced by recombinant technology. They have been in the market in the U.S. since 1989. There are four ESAs approved for this indication. All are approved for patients on and not on dialysis. All are

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administered intravenously or subcutaneously. None are oral.

Four large randomized-controlled targeted studies have shaped the labeling of ESAs: the normal hematocrit, the CHOIR, CREATE, and TREAT. They were all designed to demonstrate that higher hemoglobin targets would result in better clinical outcomes, but instead they showed, or tended to show, adverse cardiovascular outcomes with higher rather than lower hemoglobin targets. More than 30 years since the first approval of an ESA, the optimum hemoglobin target remains unknown.

In light of these prior results, the ESA label for CKD has undergone significant revisions, including the addition of a boxed warning and several warnings and precautions.

Here you see the boxed warning for the ESAs as related to chronic kidney disease. It highlights the risk of death, myocardial infarction, stroke venous thromboembolism, and thrombosis of vascular access. It also warns that targeting hemoglobin greater than 11 grams per

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deciliter increases the risk of death, serious adverse cardiovascular, and stroke. The warnings and precautions section of the ESA labeling highlights other important risks of hypertension and seizure.

After the fourth large randomized trial suggested harm rather than benefit when targeting higher rather than lower hemoglobin levels, the former division discussed the three prior results at the 2010 cardio-renal drug advisory committee meeting. We asked whether the indication for treatment of anemia in patients who are not on dialysis should be withdrawn; 15 out of 17 members voted no.

The roxadustat development program proceeded concurrently in the non-dialysis-dependent, NDD, and dialysis-dependent, DD, populations. For each patient population, there were three main phase 3 studies and one additional trial. Therefore, there was a total of four studies in the NDD indication and four studies in the DD indication.

Efficacy was assessed as the change from

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baseline in the mean hemoglobin levels over weeks 28 to 52. The study tested either superiority to placebo or noninferiority to ESA with respect to hemoglobin. For safety, the applicant assessed major adverse cardiovascular events, or MACE, comparing roxadustat to placebo in the NDD population and comparing roxadustat to epoetin alfa in the DD population. In addition, we performed typical general safety assessment of adverse events, laboratory data, and vital signs. As I noted, there were four major phase 3 studies in the NDD population. The phase 3 studies on the slide, 001 060, and 608, were similarly designed multicenter, randomized, double-blinded, placebo-controlled study in patients with stage 3 to 5 CKD and anemia. Notice that not all the randomization ratios are the same. The primary endpoint was changed from baseline to mean hemoglobin concentration. Study 610 differed in that it was conducted in

Europe with an open-label design and it compared

roxadustat to active-controlled darbepoetin alfa.

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Also for 610, the primary endpoint was different from the others. It was percentages of hemoglobin responders during the first 24 weeks.

For the DD population, there were also four major phase 3 studies. The study at the top, 002, 063, and 064, were similarly designed, multicenter, open-label, active-controlled trials that compared roxadustat to epoetin alfa. Study 002 and 063 were global and Study 064 was conducted in the U.S.

The fourth major study was 613. This study was conducted exclusively in Europe. Study 613 differed from the other three studies because it employed two active comparators, darbepoetin and epoetin alfa, and permitted use of an ESA that is licensed in the U.S. For all four studies, the primary endpoint was changed from baseline in the hemoglobin concentration.

We corroborated the applicant's efficacy results of increasing the hemoglobin and believe that the applicant has provided substantial evidence of efficacy for the indication they are seeking. Our concern about efficacy is that the

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hemoglobin concentration in the roxadustat groups in these studies tended to overshoot its target. We will start with the efficacy results for the NDD population. Here are the results for the three placebo-controlled studies. The Y-axis shows the hemoglobin concentration and the X-axis shows time in weeks. Roxadustat is shown in blue and placebo is shown in red. Note the blue arrows. All studies appear to show overshoot of the hemoglobin target followed by downward correction. The overshoots may have been related to the roxadustat starting dose, the dosing scheme, or both. One of the secondary endpoints was time to RBC transfusion. In Study 001, the time to RBC

One of the secondary endpoints was time to RBC transfusion. In Study 001, the time to RBC transfusion analysis shows a statistically significant treatment effect with a hazard ratio of 0.37. In Study 060, there was a lack of statistical significance for an endpoint more proximal in the testing sequence, so there could be no formal test of hypothesis on the time to RBC transfusion endpoint.

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The treatment effect on time to RBC 1 transfusion was nominally statistically 2 significant. In Study 610, time to RBC transfusion 3 was not included in the testing sequence. An 4 exploratory analysis indicates a nominally 5 statistically significant treatment effect. 6 The figure shows the percentages of subjects 7 who received at least one RBC transfusion in the 8 three NDD studies. The blue bars are for roxadustat and the red bars are for placebo. 10 exploratory analysis suggests that there was 11 absolute reduction in the percentages of patients 12 receiving an RBC transfusion of approximately 13 10 percent for roxadustat over placebo in each of 14 the three studies. 15 Here are the efficacy results for Study 610. 16 The study met its primary efficacy endpoint 17 18 objective in hemoglobin response. In the graph on 19 the right, note that the hemoglobin increases more

rapidly in the roxadustat group than the darbepoetin alfa group through 4 weeks; also note that the hemoglobin level reaches nearly 12 grams

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per deciliter at 12 weeks.

Now I will discuss the efficacy results for the DD population. Hemoglobin responses are shown graphically for the three studies. Roxadustat is shown in blue and epoetin alfa is shown as red. On the left top and bottom, in Study 063 and 002, you see the mean hemoglobin responses in the roxadustat groups were similar to the responses in the epoetin alfa groups.

In Study 064, which was the U.S. study, the hemoglobin in the roxadustat group trends higher than the epoetin alfa group with the mean differences of 0.5 gram per deciliter. The test for noninferiority for the difference in the hemoglobin between roxadustat and epoetin alfa of minus 0.7 gram was met for each study.

Here are the Study 613 efficacy results.

613 also demonstrated noninferiority of roxadustat with respect to ESA comparators. The graph on the right shows the mean hemoglobin response over time. The scale exaggerates the treatment effect, but note the rapid increase in hemoglobin in the

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roxadustat group starting at time zero. The

difference in mean hemoglobin response developed

rapidly with big treatment differences of

approximately 0.8 gram for roxadustat over ESA

comparator.

Now I will discuss the safety of roxadustat.

Safety analyses were performed in the NDD and DD

populations separately. The mean safety analysis

in the NDD population was conducted using the

10 4270 subjects in the three double-blind,

placebo-controlled studies, Studies 001, 060, and

608. Study 610 was analyzed separately. The main

safety analysis in the DD population was conducted

using 3880 subjects in Study 002, 064, and 063.

15 Study 613 was analyzed separately.

In order to interpret the safety analyses, it's important to understand the concept of the ascertainment window. The ascertainment window is the time on treatment plus an interval of additional monitoring time during which adverse events can be recorded. Events that occurred outside the window are not included in the

analyses.

Analyses of adverse events were conducted using three ascertainment windows. This slide depicts the on-treatment plus 7-days analysis and includes events from first day of treatment until 7 days after last dose. Similarly, the time on-treatment period plus 28 days, or OT plus 28, includes the treatment period plus 28 days after the last dose of the study indication.

The term "on-study" includes all adverse events that occurred after randomization until the end of the study, regardless of whether the patient was on or off study treatment. You can understand that the longer the period of observation, the more likely you are to collect adverse events that occurred after drug exposure and are not drug related, but for adverse events with longer latency, it's important to monitor for a longer duration. The optimal ascertainment window can differ depending on the type of adverse event that is being considered.

For the most part, our safety analyses were

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conducted using queries. These included a combination of medically similar and/or related preferred terms. The FDA is developing a standard set of custom queries for new drugs. For example, the FDA query for acute kidney injury is shown in the left. All of these terms indicate a reasonable likelihood that acute kidney injury occurred. An example of custom query of device/shunt thrombosis is shown on the right and it includes 10 related preferred terms that all denote device or shunt thrombosis.

Now we will discuss the adverse events starting with the NDD population. We are not showing the data by treatment group, but for each of the pooled NDD studies, the demographic and baseline disease characteristics generally well balanced between the two treatment groups.

Overall, the mean age was 63 years. The majority of patients were female and overall white. Note, approximately 8 percent of the study population were black. U.S. participation varied by study but overall about a quarter of patients

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were from the U.S. Few patients had received prior ESA treatment. One-third had a known history of cardiovascular disease.

There were significant differences in disposition between the roxadustat and placebo groups. Thirty-eight percent of subjects in the roxadustat groups discontinued treatment early versus 59 percent of subjects in the placebo groups. The difference was driven by the need for rescue therapy and subjects' decisions differing by about 10 percent.

This Kaplan-Meier graph illustrates the differences in drug exposure between the roxadustat groups in blue and placebo groups in red. The mean roxadustat exposure was 85 weeks compared to 64 weeks for placebo. The lines diverge from each other and reach peak difference at 52 weeks, at which time 71 percent of patients in the roxadustat groups and 53 percent of patients in the placebo groups remained on treatment.

Now I will begin the presentation of the adverse events in these studies. Realize that we

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looked for hundreds of signals in two groups of three studies and two individual studies. Signals that were observed across more than one analysis or study are more likely to be drug related. This is a tabulation of serious adverse events organized by category.

The listings are mostly adverse event queries, although there are a few individual preferred terms as well. Individual terms are followed by word terms. For example, deep vein thrombosis is an individual term, though it falls within the query of thrombotic events.

These two columns show the numbers and percentages of subjects with events. These two columns show the event rate per patients-years. The column with the red bars shows the risk difference per 100 patient-years. Finally, the column with the blue bars shows the relative risk based on patient-years.

The listed adverse events and queries are those that were reported at a rate of at least 0.5 events per 100 patient-years with roxadustat,

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with a relative risk of at least 1.3. Others are listed because they were of particular interest. The ascertainment window here is on treatment plus 7 days. Roxadustat shows a clear signal for serious thrombotic events with a relative risk of 1.45. Important serious adverse events that contribute to this query include device/shunt thrombosis with a relative risk of 2.7 and deep vein thrombosis where there are 20 versus 2 events and a relative risk of 6, also. Stroke and pulmonary embolism, keep in mind that the absolute risk of device/shunt thrombosis is underestimated here because most of these patients in these studies were not on dialysis. Other identified signals include intracranial hemorrhage and seizures. The risk of serious infection includes increased risk for septic shock; urinary tract infection; bacterial infection as a general category; and peritonitis. In contrast to the placebo-controlled studies, Study 610 compared roxadustat to darbepoetin alfa. Again, note the serious adverse

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events of infection, including bacterial infection and pneumonia were reported, higher percentages for roxadustat than darbepoetin alfa, and with a relative risk of 1.3 or greater. The thrombotic risk is a particular concern here because roxadustat was compared to darbepoetin alfa, which itself is known to cause thrombosis.

Now we will examine all adverse events in the NDD pooled studies for serious and non-serious adverse events. Again, we are showing results for analyses based on the OT-plus-7 window, and here we show events where the rate was greater than 2 per 100 patient-years in the roxadustat group and where the relative risk was greater than 1.2.

There are some adverse events of particular interest. Again, there are notable signals for thrombosis and sepsis although the majority of these events were serious in nature and were shown in the last tabulation. In other words, most adverse events of thrombosis and sepsis were serious. There were relatively few non-serious events.

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So if we focus on the other adverse events that are largely non-serious, we see hyperkalemia nausea, vomiting, insomnia, and peripheral edema. There are also far more seizures here, indicating that many seizures were non-serious.

For Study 610, we see the adverse events
that occurred at a frequency greater than 5 percent
in the roxadustat arm. Again, there are signals
for peripheral edema and fluid overload and also
for thrombosis, insomnia, and nausea as we saw in
other studies in the NDD population. The new
signals observed in this study included
hyperphosphatemia; muscle spasms; dyspnea; also
arrhythmia; constipation; headache; hypotension;
and bronchitis.

Now I will discuss the adverse events in the dialysis population. We are not showing the data by treatment arm, but the baseline demographics and disease characteristics where relatively well balanced between treatment arms for the dialysis-dependent population.

The mean age was 54 years overall. Most

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patients were male and overall white. Overall, approximately 45 percent were from the U.S., although all subjects in Study 064 were from the U.S. Almost 90 percent were on hemodialysis and 43 percent had a history of cardiovascular disease.

In the pooled DD population, the rate of early discontinuation was higher in the roxadustat group than the epoetin alfa group, 42 percent versus 34 percent. The reasons for discontinuation were adverse events and subject or physician decision to leave the study.

This Kaplan-Meier graph illustrates study drug exposure for the DD population, with the blue line representing roxadustat exposure and the red line representing epoetin exposure. Mean exposures were 89 weeks in the roxadustat-treated subjects and 101 weeks in epoetin alfa-treated subjects.

Approximately 63 percent and 71 percent of patients in the roxadustat and epoetin alfa groups, respectively, received the study drug for at least 52 weeks.

This table shows serious adverse events for

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the pooled studies in the DD population. We have tabulated adverse event queries and some individual adverse event terms, where the event rate was greater than 0.5 per 100 patient-years and the relative risk was at least 1.3, as well as some other notable signals.

Because roxadustat was compared to an active ESA control group in these studies, it's important to consider known adverse drug reactions of ESA when assessing roxadustat's risks. Thus, we show the known adverse drug reaction for ESA at the bottom of the table.

Again, you see prominent signals of serious thrombotic events, including device or shunt thrombosis, deep vein thrombosis and myocardial infarction, as well as seizure.

It's important to recognize that these signals appear against epoetin alfa as the comparator rather than placebo, and note that thrombosis, MI, and seizures are listed as adverse drug reactions in ESA labeling. Signals for adverse events of hypoglycemia, gastroenteritis,

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and pancreatitis are evident here although they were not detected in the in NDD studies.

Now for the single study in the DD population, Study 613, as you recall, Study 613 compared roxadustat to an ESA group that included darbepoetin alfa and epoetin alfa, and this study was not included in the pooled analyses. This table lists the serious adverse events that occur at a frequency greater than 5 percent in the roxadustat group, with a relative risk that exceeded 1.3 in Study 613.

Notable serious adverse events include congestive heart and thrombosis of vascular access. Both are listed as an adverse drug reaction in the ESA level. In addition, there is a risk of serious infection, which was also observed in the pooled NDD analyses.

Here are all adverse events in the pooled DD studies for the OT-plus-7 time period for serious and non-serious. The table shows adverse event queries reported at a rate of greater than 2 per 100 patient-years in the roxadustat group,

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where the relative risk for roxadustat was greater 1 than 1.3. Other notable adverse events are shown 2 as well. The thrombotic event shows up as 3 expected, however, most of these events were 4 serious such that the addition of non-serious 5 events here does not add much information. 6 Seizures shows up again in the serious 7 adverse events, however, almost half of the 8 seizures were non-serious. Again, seizures are 9 labeled adverse drug reaction for ESAs. There is a 10 signal for vomiting, which is consistent with the 11 signal observed in the pooled NDD analysis. Small 12 signal for hypertension, peripheral edema, and rash 13 14 are apparent versus ESA, and they are labeled adverse drug reactions for ESAs. 15

Again, we see a signal for thrombosis. Sorry.

This slide shows all adverse events identified in Study 613 with a frequency greater than 5 percent in the roxadustat group and a relative risk that exceeded 1.3, as well as other significant adverse events.

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Again, we see a signal of thrombosis with roxadustat, which included deep vein thrombosis, pulmonary embolism, and device/shunt thrombosis.

Contrary to other studies in the DD population, MI and ischemic stroke favors roxadustat over ESA and are shown for completeness. There are signals for nausea and congestive heart failure in the study that are similar to those observed in other studies.

Given the strong signals of thromboembolic events, here are the Kaplan-Meier curves of all thromboembolic adverse events for the NDD population on the left and DD population on the right. These analyses are based on on-study assessment window.

The curves in the NDD population are

difficult to interpret because of the marked

differences in subject retention between the two

groups. For the DD population, however, time at

risk was similar in both groups, and about

90 percent of patients were on hemodialysis with

vascular access. Roxadustat risk of thromboembolic

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events versus ESA is quite clear in this population. The log-rank test show nominally statistically significant results for both analyses.

Vascular access is the lifeline for hemodialysis patients. Here are the Kaplan-Meier curves for device and shunt thrombosis in the DD population. These analyses are based on the on-study ascertainment window. On the left, the figure shows all of these adverse events for serious and non-serious. On the right, only the serious events are shown.

They both show events through 36 months or 3 years. I will remind you that the absolute risk difference for all of these events was 2.1 events per 100 patient-years, and for serious adverse events, it was 1.1 event per 100 patient-years.

The vast majority of patients who developed serious events of device/shunt thrombosis required hospitalization and placement of a new vascular access.

Now, Dr. Song will present the MACE results.

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Presentation - Jae Joon Song

DR. SONG: Good afternoon. My name is

Dr. Jae Joon Song, and I am a statistical reviewer

in the Office of Biostatistics. In this

presentation, I'm going to discuss the

cardiovascular safety analysis and results. I will

also explain the differences and implications of

using on-treatment and on-study analysis.

In the cardiovascular safety evaluation,

MACE was defined as a composite of all-cause

mortality, non-fatal myocardial infarction, and

non-fatal stroke. Study endpoints were adjudicated

by an independent clinical endpoint committee whose

members were blinded to treatment assignment.

One of the key analytical considerations was how the MACE event will be counted with respect to the exposure to treatment. An ascertainment window defines period of time for which a subject is at risk of the event and determines which events will be considered in analysis.

For the MACE analysis, we considered two windows, on treatment plus 7 days, or OT plus 7,

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and on-study analysis. The two ascertainment windows can have different implications on the interpretation of results. In the following slide, I will explain the definition and differences in these two approaches to set the stage for discussing the MACE results from the roxadustat trials.

A key issue in the assessment of safety in the roxadustat program is when a safety event occurs relative to exposure to treatment. This slide includes an illustration of hypothetical subjects and time they're being followed in a trial.

The green line depicts a time a subject is exposed to randomize treatment. The gray line depicts the ascertainment window after treatment exposure, which in this program was commonly defined as 7 or 28 days. The dash line depicts time while a subject was off treatment but still being followed for the event of interest.

Events are depicted with red diamonds. As mentioned, the assessment of MACE used two exposure

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windows. What is depicted here is the OT-plus-7 analysis, which includes only events that occur within or prior to the end of the ascertainment window. Subjects not experiencing event within this time frame are censored at the end of the ascertainment window.

For the previous hypothetical example, only two events were contributed to the OT-plus-7 analysis. As shown in the illustration, the on-treatment or the OT-plus-7 analysis estimates risk of MACE in patients assigned to roxadustat while receiving the assigned treatment.

This slide depicts the on-study analysis.

In such an analysis, all events are included regardless of exposure to treatment. Subjects not experiencing an event are censored at the date of last contact. Per our hypothetical scenario, you can see two additional events contribute to the on-study analysis relative to the on-treatment analysis.

As shown in the illustration, the on-study analysis, or the treatment policy analysis,

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estimates the risk of MACE in patients randomized to roxadustat versus control regardless of treatment adherence, discontinuation, or use of alternative therapies.

Having introduced the concept of
on treatment versus on-study analysis, I now will
discuss how these analyses estimate two different
risks. In the interpretation of the estimates of
risk observed in the roxadustat development
program, it is important to understand the pros and
cons of the two analysis approaches, which I will
discuss in the next set of slides.

The first estimate which I discussed is on treatment, which estimates the risk of MACE while receiving the assigned treatment. In general, there is increased sensitivity to see drug effects with the on-treatment estimate if drug attributable risk only occurs while a subject is exposed to randomize treatment. However, the on-treatment analysis can be difficult to interpret when there is considerable disparity between treatment arms on how long subjects remain on treatment.

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In other words, if there is differential treatment discontinuation between the treatment arms and if there's a reason to suspect that the differences might be related to the outcome of interest, then there is potential for obtaining a biased estimate. Finally, the on-treatment analysis is also not suitable for assessing risk and outcomes expected to have long latency.

Now for the on-study analysis, this estimate may be important if the control arm receives a reasonable representation of current standard of care. In this setting, the treatment policy approach can help assess what might happen to the target population with respect to the outcome if the investigational product is approved for marketing. Also, the on-study approach may provide greater sensitivity to adverse effects and outcomes with potentially long latency periods such as malignancy.

However, the on-study approach can be less sensitive to identifying drug attributable risk when outcomes occur after treatment

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discontinuation, and this can be especially concerning in the noninferiority settings because with more unexposed time, the on-study analysis is more likely to show noninferiority. Moreover, in the presence of a rescue therapy, the unexposed time to plan treatment can include exposures to rescue therapies, which might impact the comparisons of risks.

Finally, the quality of the on-study analysis relies on how well subjects were followed up, so there can be interpretability issues when there are systematic differences between treatment arms and follow-up time.

In the assessment of MACE in all-cause mortality you will see that results depend on how the data were analyzed, and specifically whether the time of observation was limited to time on treatment or extended to last contact. It is important to consider these pros and cons of the analysis when interpreting the safety results.

As shown earlier in Dr. Ayache's presentation, overall in the NDD trials, subjects

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in the placebo arm tended to discontinue treatment 1 Notable in this Kaplan-Meier plot is a 2 early. period after randomization to week 52 where 3 subjects randomized to placebo arm appeared to have 4 discontinued treatment in a more rapid pace 5 compared to roxadustat. Such differential 6 7 treatment duration poses a challenge in the interpretation of the on-treatment analysis. 8 Specifically, the risk estimated using the 9 OT-plus-7 (analysis) might be biased, (for example, if 10 the patient on the placebo arm, who are at greater 11 underlying risk of MACE, tend to discontinue 12 treatment early. In the DD trials, overall there 13 14 were more roxadustat subjects who discontinued treatment early, however, the discontinuation pace 15 was roughly constant shortly after randomization. 16 I will now describe the methodology used to 17 18 analyze MACE. The objectives of the MACE analysis 19 were to demonstrate noninferiority in CV risk of roxadustat compared with placebo in the NDD 20 21 population. In the DD population, the objectives of the MACE analysis were to demonstrate 22

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noninferiority and CV risk of roxadustat compared 1 to ESAs. 2 I'll note the applicant and FDA did not 3 agree prospectively on a risk margin. Furthermore, 4 we do not agree with the applicant's proposed 5 margin of (1.3, as (it) was defined after results of 6 7 the study were known. Therefore, FDA does not agree on the interpretation of the results using 8 strictly a noninferiority hypothesis testing 9 approach. Rather, our interpretation of the trial 10 findings focuses on the estimation of MACE risk and 11 the uncertainty around it. 12 Such statistical inference appear to be 13 14 appropriate because the development programs for both populations were sufficiently large to observe 15 a meaningful number of CV events to estimate the 16 risk, and the definition and data capture of the 17 18 outcomes was of high quality. 19 For evaluation of CD safety in the NDD population, three phase 3 randomized, double-blind, 20 21 placebo-controlled trials were prospectively agreed upon. In addition, there were three phase 3 22

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randomized open-label ESA-controlled trials that were prospectively agreed upon for evaluation of safety in the DD population.

The primary analysis for the NDD population was on-study with a sensitivity analysis performed as an on-treatment analysis. For each trial, Cox regression was used to model the treatment effect using prespecified trial-specific stratification factors. Hazard ratios from each trial were combined using weight inversely proportional to the variance of the study-specific log hazard ratio estimates.

The primary analysis for the DD population was on treatment with a sensitivity analysis performed as on-study analysis. Similar to the meta-analysis for the NDD population, Cox regression was used to model the treatment effect for each trial using prespecified, trial-specific stratification factors. The overall hazard ratio estimate was obtained using a meta-analysis technique that's previously described for the NDD population.

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Now I will provide a summary of the MACE analysis results in the in NDD population. Presented in this slide are Kaplan-Meier curves for the analysis of MACE in the NDD population. In the primary on-study analysis, the hazard ratio comparing the risk of MACE between roxadustat and placebo was 1.1 with a 95 percent confidence interval that ranged from 0.96 to 1.27. There was considerable difference in the hazard ratio estimate using on-treatment or OT-plus-7 analysis, with a hazard ratio of 1.38 and a 95 percent confidence interval that ranged from 1.1 to 1.7. Results for components of MACE is presented in this table for the on-study and all OT-plus-7 analyses. As you can see, most of the MACE events were driven by all-cause mortality, which I will discuss in more detail in a later section. In the ESA control trial 610, not considered for the meta-analysis, the estimated hazard ratio comparing roxadustat to darbepoetin alfa in the on-study analysis was 0.89 with a 95 percent

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confidence interval that ranged from point 0.6 to 1.3. In the OT-plus-7 analysis, the hazard ratio was 0.7 with a 95 percent confidence interval that ranged from 0.44 to 1.2.

In summary, there was considerable difference between the estimated hazard ratios for the primary on-study analysis and the OT-plus-7 sensitivity analysis. In the NDD population, the treatment policy analysis results suggest no significant difference in the risk of MACE relative to placebo. On the other hand, the results from the on-treatment or the OT-plus-7 analysis suggest an increased risk of MACE for the roxadustat arm compared to placebo.

Although the 95 percent confidence interval for the OT-plus-7 analysis merits concern, the differential exposure between roxadustat and placebo complicates the interpretation of the OT-plus-7 analysis in isolation, as this may not represent a fair randomized comparison.

Now I will provide a summary of the MACE analysis results in the DD population. In the

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primary on-treatment or OT-plus-7 analysis, the hazard ratio comparing the risk of MACE between roxadustat and ESA was approximately 1 with a 95 percent confidence interval for the estimate, ranging from 0.88 to 1.2.

On the other hand, the on-study analysis indicated a higher risk of MACE in subjects randomized to roxadustat, with a hazard ratio of 1.14 and an upper bound of the 95 percent confidence interval 1.3.

Results for the components of MACE are presented in this table for both OT-plus-7 and on-study analysis. As you can see, a majority of MACE events were driven by all-cause mortality, which I will discuss in more detail in a later section.

In the ESA-controlled trial 613, not considered for meta-analysis, the estimated hazard ratio comparing roxadustat to ESAs were 1.29 in the OT-plus-7 analysis, with a 95 percent confidence interval that ranged from 0.91 1.85. The on-study analysis suggested an increased risk of MACE, with

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a hazard ratio of 1.39 and a 95 percent confidence interval that ranged from 1.01 to 1.91.

In summary, in the DD population, results suggested no significant difference in the risk of MACE while subjects were receiving the assigned treatment. However, the on-study analysis suggests an increased risk of MACE relative to ESA, and the direction of such risk was also consistent in a trial that was not considered for meta-analysis.

As discussed earlier in my presentation, it is important to remember that on-study analysis represents an estimate of the treatment policy principle that compares the risk regardless of treatment adherence, discontinuation, or use of alternative therapy.

Now I will provide a summary of the all-cause mortality analysis results in the DD population. In the on-study analysis, the hazard ratio comparing the risk of all-cause mortality in subjects randomized to roxadustat compared to placebo was 1.08 and the 95 percent confidence interval ranged from 0.93 to 1.26.

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There was considerable difference in the hazard ratio estimated using an OT-plus-7 analysis, with a hazard ratio 1.40 and the 95 percent confidence interval that ranged from 1.08 to 1.82. Causes of death were adjudicated by an independent event committee. In the OT-plus-7 analysis, fewer than half of deaths were cardiovascular in nature. Overall, the leading causes of death were infections, renal death, and sudden cardiac death. In the ESA-controlled trial 610, not considered for meta-analysis, hazard ratios comparing the risk of death between subjects randomized to roxadustat and darbepoetin alfa were 0.94 and 0.67, respectively, for on-study and on treatment plus 7 analysis. However, the number of deaths were considerably smaller in the meta-analysis, which results in more uncertainty in the risk estimates. Now I will provide a summary of the all-cause mortality analysis results in the DD population. In the on-study analysis, the results suggested higher risk of all-cause

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mortality relative to epoetin alfa, with a hazard ratio of 1.17 and the 95 percent confidence interval that ranged 1.02 to 1.35. On the other hand, in the OT-plus-7 analysis, the hazard ratio for comparing the risk of all-cause mortality between roxadustat and epoetin alfa was 1.02 and the 95 percent confidence interval that ranged from 0.85 to 1.23.

More than half of the deaths were

More than half of the deaths were cardiovascular related. The leading causes of cardiovascular death were acute MI and sudden cardiac death. The leading non-cardiovascular causes of death were infections and renal death.

In trial 613 that was not considered for meta-analysis, the risk of all-cause mortality appeared to be higher for the roxadustat arm compared to ESAs. The estimated hazard ratio comparing roxadustat to ESAs in the on-study analysis was 1.54 with a 95 percent confidence interval that ranged from 1.09 to 2.16. In the OT-plus-7 analysis, the estimated hazard ratio was 1.54 with a 95 percent confidence interval that

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ranged from 1.04 to 2.28.

Now Dr. Ayache will provide a summary of analyses exploring the relationships between thromboembolic events, roxadustat dose, hemoglobin, and hemoglobin rate of change.

Presentation - Saleh Ayache

DR. AYACHE: This slide illustrates the relationship between thrombotic events and overall weight adjusted roxadustat dose. The mean, study drug dose was calculated for each subject in the pooled analyses and subjects were arranged in quintiles on the basis of total dose and treatment group.

For these slides, Q1 represents the lowest quintile and Q5 is the highest. The number of thromboembolic events were calculated for each dose quintile and expressed as percent of subjects with events. The number inside the bars represent the numbers of events. The black bars are roxadustat and the open bars are the comparators. Analysis for the NDD and DD populations are shown on the left and right, respectively.

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We see weak association between the total weight adjusted roxadustat dose and probability of thromboembolic events. There is no clear association in subjects who receive ESA. Given that the doses of study agents were titrated and changed throughout the study, it makes more sense to assess thrombosis rate on the basis of the drug doses received at the onset of the event.

This slide illustrates this relationship for the NDD on the left and DD population on the right.

This figure suggests a fairly strong association between the roxadustat dose and thrombotic events, but no association in the placebo-treated patients.

The right figure for the DD population shows a reasonable association for subjects who received roxadustat but no clear association for subjects who received ESA. An important point should be made here. Because the doses were titrated based on the hemoglobin response, the analysis is confounded by responsiveness. In other words, the doses tended to be increased to a greater extent in subjects who were poorly responsive to the drug.

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Thus, the bars in the higher quintile -- Q3, Q4, and Q5 -- includes disproportionately more subjects who were poorly responsive to the drug. Such patients have more advanced kidney disease as well as a greater burden of concomitant diseases. As such, there were a greater risk of cardiovascular and thrombotic events. It's not possible to separate these factors. Here you see the relationship between the thromboembolic events and hemoglobin in the NDD population on the left and the DD population on the Hemoglobin values were estimated for all subjects for all weeks in treatment and patient-weeks were based in quintiles on the basis of hemoglobin concentration separately by treatment arm. The numbers of thromboembolic events were assessed for each quintile for both treatment arms and expressed as a rate per 52 patient-weeks. Q1 represents the lowest quintile and Q5 is the highest.

A number of prior studies have suggested

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that subjects with lower hemoglobin values are at a higher risk of cardiovascular events, and such an association was observed here as well. The question always arises as to whether the higher risk is related to the lower hemoglobin values per se, or whether lower hemoglobin is a marker of more advanced kidney disease and more concomitant disease, which renders patients less responsive to hemoglobin stimulating drugs are more likely to experience adverse events. It's not possible to separate these factors easily.

This slide illustrates the relationship between thromboembolic events and hemoglobin rate of rise. The hemoglobin rate of rise was estimated for each week that each patient was on treatment by fitting a linear regression line through the hemoglobin values obtained during the preceding 4 weeks.

Patient-weeks were placed in quintiles.

Adverse events were tabulated for each quintile for both treatment arms and results are expressed, thrombotic events per 52 patient-weeks. Q1

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represents the lowest quintile and Q5 is the highest.

Note that the numbers of the events are very small, particularly on the left figure. The numbers are limited because a slope could not be calculated for many patients-weeks. Nevertheless, in both populations there are apparent associations between thrombotic events and hemoglobin rate of rise.

Such associations were also found in the darbepoetin alfa development program. While the analysis I just displayed showing thrombotic events versus hemoglobin concentration was confounded by responsiveness, this analysis is not.

Specifically, patients who are more responsive to these drugs tend to achieve higher rates of hemoglobin rise, and one might reasonably ask whether these thrombotic events tended to occur near the beginning of the studies when the hemoglobin tended to rise most rapidly.

However, the Kaplan-Meier curves shown in slide 44 show that these thrombotic events tended

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to occur throughout these studies and not mostly at the beginning. Although these data are not conclusive, it's possible that limiting hemoglobin rate of rise could decrease the incidence of thromboembolic events.

In summary, the clinical trials in NDD and DD populations showed that roxadustat is effective in increasing the hemoglobin level. Exploratory analyses show an absolute reduction of RBC transfusion of approximately 10 percent compared to placebo.

Roxadustat is administered orally, which may offer an advantage over ESAs, which are administered IV or SubQ. If such an advantage exists, it would be for patients who do not receive hemodialysis. Importantly however, hemoglobin intended to overshoot target in the NDD population and in Study 613, and its relation to risk is uncertain.

The risk of MACE and all-cause mortality are difficult to interpret. The primary analyses were neutral when comparing roxadustat to placebo in the

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NDD population and roxadustat to ESA in the DD population, however, the sensitivity analyses in both populations were unfavorable for roxadustat.

There are higher risks for roxadustat than both placebo in the NDD population and epoetin alfa in the DD population for thrombosis, vascular access thrombosis, and seizure. There appears to be higher risk than placebo in the NDD population and a similar risk to epoetin alfa in the DD population for myocardial infarction, stroke, and systemic hypertension. Also, there appears higher risk of serious and fatal infections than placebo in the in NDD population.

This concludes our talk. Thank you for your attention.

Clarifying Questions

DR. LEWIS: We will now take clarifying questions for FDA. Please use the raised-hand icon to indicate that you have a question and remember to put your hand down if you have asked your question.

When acknowledged, please remember to state

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your name for the record before you speak and 1 direct your question to a specific presenter, if 2 If you wish for a specific slide to be 3 displayed, please let us know the slide number, if 4 possible. Finally, it would helpful to acknowledge 5 the end of your question with a thank you and the 6 end of your follow-up question with, "That is all 7 for my question," so we can move on to the next 8 9 panel member. 10 I will reserve the unasked clarifying questions for the sponsor for later, so this now 11 opens the clarifying questions for the FDA. 12 Mr. Conway? 13 14 (No response.) DR. LEWIS: Mr. Conway, you may be on mute. 15 MR. CONWAY: Thank you very much; a general 16 question for FDA. 17 18 I've had a concern in looking at the data in 19 the summary, which I think was very detailed, about pooled data in general. Can you tell me for 20 21 first-in-class drug consideration, how common is that? And for this particular set of data, the 22

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pooling, is that common or was this novel in
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     putting it together like this? Either presenter;
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                  That's my question.
3
      thank you.
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             DR. LEWIS: FDA?
              (No response.)
5
             DR. LEWIS: Do one of the FDA speakers, or
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7
     another member of the FDA present, want to answer
      that question?
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             DR. YU: Could Dr. Song answer the question?
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             DR. LEWIS: Dr. Song, you may need to
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     unmute.
11
                        This is Dr. Song, FDA.
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             DR. SONG:
     MACE analysis, actually the data weren't pooled.
13
     The hazard ratios estimated at each trial level
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     were combined using a meta-analysis technique.
15
                                                       As
      for the MACE analysis and all-cause mortality
16
      analysis, the hazard ratio estimates were based on
17
18
     meta-analysis.
19
             MR. CONWAY:
                          Thank you.
             DR. LEWIS: Did that answer your question,
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21
     Mr. Conway? Because I think the question is for
      first-in-class drugs; do you do this with pooling
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data or one defining study, looking at
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     cardiovascular safety? For example, MPEG reg [ph],
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     which is more common.
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              (No response.)
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             DR. LEWIS: Dr. Song?
5
              (No response.)
6
7
             DR. LEWIS: Does any member of the FDA want
      to further comment?
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9
             DR. UNGER: Yes. This is Dr. Unger.
      jump in. I think the question, if I interpreted it
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      correctly, was more about the standard safety
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      analyses.
                 I think the answer is this was quite a
     wide and deep development program.
                                           It's not
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14
      typical that we get six trials, or more, to support
      the efficacy and safety of a drug.
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             But when we get trials that are similar in
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      design, for any indication, for safety analyses, we
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      do tend to pool. We tend to use simple pooling
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     when we can.
                    So it's not unusual for a development
     program to have this many trials, but it's somewhat
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21
     unusual to have a development program that has this
     many trials. I hope I've answered your question.
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MR. CONWAY: You have. Thank you very much. 1 DR. LEWIS: Thank you, Dr. Ellis. 2 Dr. Cho? 3 DR. CHO: Yes. This is Leslie Cho. Thank 4 you for the nice analysis, and two questions for 5 the FDA. 6 One is, as far as all the roxadustat 7 studies, it appears that they've excluded patients 8 with history of cancer, especially hematological 9 cancer, and then they've excluded patients unless 10 they were cancer-free for 5 years. 11 Is this correct? 12 DR. FARRELL: Yes, some of those. I'd like 13 14 to refer, though, the question to the sponsor because they have a significant database in many 15 countries. 16 DR. LEWIS: Okay. 17 18 DR. CHO: And then my second question is, 19 there was a lot of mention from the sponsors regarding hyporesponse to the epo, to the ESA 20 21 class. Is there any data from the sponsor regarding the hyporesponders' response to their 22

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drug? 1 DR. LEWIS: I quess those two questions are 2 actually to the sponsor; is that correct? 3 I'll let the sponsor answer. 4 DR. EISNER: Dr. Lewis, it's Mark Eisner. 5 Do you want us to address those questions now or 6 later? 7 DR. LEWIS: Yes, you can do it now since we 8 asked them right now. 9 DR. EISNER: Okay. Let me ask Dr. Little to 10 address your question about history of cancer, and 11 12 then Dr. Szczech to answer the question about hyporesponse. 13 DR. LITTLE: Dustin Little here. 14 Dr. Cho, across the program, in general, 15 patients with a history of prostate cancer, breast 16 cancer, or other malignancies were excluded with 17 18 the exceptions of cancers determined to be cured or 19 in remission for five or more years, or curatively resected basal cell or squamous cell cancers, 20 21 cervical cancer in situ, or resected colonic polyps. 22

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DR. CHO: But all hematological cancers 1 appears to be one of the contra-exclusion criteria 2 is that correct? 3 DR. LITTLE: Yes, that would have been 4 considered an exclusionary Criterion. 5 DR. CHO: And the reason I ask is because I 6 am concerned about the increased rate of thrombosis 7 seen. And it may not be related to the rise of 8 hemoglobin but may be related to the class of drug 9 10 itself, and that is the reason for the question. Thank you. 11 12 DR. LEWIS: Thank you. Dr. Moliterno? 13 14 DR. MOLITERNO: Thank you, Dr. Lewis. if you want to deem this question better for later, 15 that's fine because it's concerning a little bit of 16 the question I had earlier. 17 18 For the sponsors or to the FDA, I think many of us on the call understand the foundational 19 concepts of pros and cons we're considering, but 20 what I haven't heard much discussion from either 21 side so far is this risk mitigation modeling and 22

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potential statistical shortfalls with some of the,
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      I guess, assumptions or speculations.
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             So I'm wondering if now or later, Dr. Song,
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     Ayache, or perhaps Dr. Unger, want to make any
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      comments, or if we want to wait until later.
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             DR. LEWIS: I think those questions can be
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      answered by the FDA now.
             DR. UNGER: This is Dr. Unger. In terms of
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     both changing the paradigm for dosing and in terms
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      of the proposal for a postmarketing study, those
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     were put on the table by the applicant fairly
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      recently, and we have not had a chance to discuss
      them or analyze them. So they are not something we
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      can discuss. Thank you.
             DR. LEWIS:
                          Thank you. It's something maybe
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     we can discuss in the discussion section.
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             DR. MOLITERNO: Yes. I agree completely.
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             And just maybe a clarifying question, not to
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      that one; but is it correct that mortality data or
      long-term survivorship was missing in roughly
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      10 percent of the population studied?
                         That's a question for the FDA?
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             DR. LEWIS:
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DR. MOLITERNO: Well, the FDA didn't comment 1 on it, except in the very early part, but they 2 didn't address it specifically. I'm happy to have 3 either side, any concerns. I appreciate that it 4 was balanced between the groups, but it seems like 5 there was around 10 percent missing data for 6 mortality or survivorship, which is quite 7 surprising given the illness of this cohort. 8 DR. FARRELL: This is Dr. Farrell. 9 Would the applicant please respond to the 10 question? 11 DR. EISNER: Yes. Let me ask Dr. Little to 12 respond to your question about the follow-up 13 completeness for all-cause mortality. 14 Dr. Little? 15 DR. LITTLE: Dustin Little. We did have 16 91 percent of patients complete follow-up for 17 18 all-cause mortality in the NDD pool and 91 to 19 92 percent of patients completed follow-up for all-cause mortality in the DD pool. 20 21 If I may, I'd like to take just 20 seconds and then show a quick comparison of how the 22

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treatment completion and study completion rates in
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     our trials compare to CKD anemia trials that came
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     before us.
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             On the left is percent of patients with
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      treatment completion, and roxadustat is the yellow
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      dots, and then on the right is percent of patients
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     with study completion. Perhaps due to the high
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      comorbidity in these patients, historically, the
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     retention rates are lower than cardiovascular
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      safety trials in other outcomes, and in general we
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     had comparable rates of treatment and study
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     completion compared to the trials that came before
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     us.
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             DR. LEWIS:
                          Thank you.
             Dr. O'Connor?
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              (No response.)
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             DR. LEWIS: Dr. O'Connor, you may be on
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     mute.
             I actually don't see him on our list, so
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     we'll go on to Dr. Wang and come back to
      Dr. O'Connor.
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             Dr. Wang?
             DR. WANG: Yes. Thank you.
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                                            The FDA
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speakers nicely showed how the results differ by ascertainment interval, which I know would be a subject of a lot of conversation.

If the FDA speaker could clarify, what was marked as the primary analysis differed in the NDD versus DD populations with the on-study interval chosen for the NDD population but the on-treatment plus 7 chosen for the DD.

Was that decision made by the FDA, was it made in discussion with the sponsor, or was it proposed by the sponsor and approved by the FDA?

And secondly, was the timing of that decision at a point in time when the data had already been acquired or was it prespecified?

DR. FARRELL: This is Dr. Farrell. These were discussed with the sponsor during the various sponsor meetings that we have had. Some of it had to do with when we thought for the dialysis population they would likely need to go back on to an ESA once roxadustat was stopped. So those were some of the considerations.

Does this answer your question?

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DR. WANG: Well, if I could follow up; so 1 that was not fully discussed? It sounds like that 2 was an ongoing dialogue. I guess secondly, if you 3 could just clarify, why was a different interval 4 chosen for the NDD versus DD populations? 5 DR. FARRELL: Most of the conversations 6 7 occurred pre-data --DR. WANG: Okay. 8 9 DR. FARRELL: -- pre-data. And again, it was a consideration about one patient on dialysis 10 would be likely needing to start therapy. 11 also based on what we had seen in the Omontys 12 program, as well as TREAT and CHOIR. 13 14 These conversations were a long time ago, and I would ask the sponsor if they have a better 15 recollection of why some of the time points were 16 chosen. 17 18 DR. EISNER: Yes. Mark Eisner. If I may, 19 we agree with you, Dr. Farrell. The primary analysis for NDD and MACE was the on-study or 20 21 intention-to-treat analysis to take care of the bias introduced by informative censoring. And for 22

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the dialysis-dependent population, we both agreed
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      that the OT7 was a preferred window for the reasons
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     you stated about switching to ESA after
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     discontinuation of roxadustat.
             DR. WANG:
                        Thank you.
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             DR. LEWIS: Dr. Thadhani?
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             DR. THADHANI: Dr. Lewis, my question was
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      identical to the previous one from Dr. Wang.
                                                     Thank
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9
     you, Dr. Lewis.
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             DR. LEWIS:
                          Okay. Ms. Alikhaani?
             MS. ALIKHAANI: Yes. Jacqueline Alikhaani
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             I don't know if this question was answered
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     before, but it's really for the sponsor.
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     wanted to get a little information about the reason
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      that the data was not generated showing that
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     patients that are hyporesponsive to ESAs are
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      responsive to roxadustat.
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             So I don't know if I missed that
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      information, but can the sponsor answer that for me
     now?
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             DR. EISNER: Yes. Thanks. It's Mark
     Eisner. I'll ask Dr. Szczech to address your
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question about hyporesponsiveness to ESA and the 1 role for roxadustat. 2 Dr. Szczech? 3 DR. SZCZECH: Thank you very much. 4 I hope that the slide that I just asked 5 Szczech. to be pulled up will be pulled up. 6 7 During the presentation, we presented data on CRP, ferritin, and hepcidin as present in your 8 briefing book, looking at the mechanistic causes of 9 hyporesponsive. But anticipating your question 10 about who were hyporesponsive at baseline, we can 11 go to the stable dialysis population, those 12 patients that converted from ESA to roxadustat, and 13 14 look at the relative hierarchy of their responsiveness as they made that conversion. 15 So yes, this slide is up. I just did a 16 quick technical check. On the left, you see 17 18 patients treated with ESA; on the right, you see 19 patients treated with roxadustat. The patients in this slide were selected because they converted 20 21 from one trial to another, therefore allowing us to make this comparison. 22

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We stratified on baseline hemoglobin, which is one of the criteria for hyporesponsive, that you don't get the response that you want, therefore, your hemoglobin is not as high as you'd like it to As you look from left to right in the graph on be. the left of ESA-treated patients, the hierarchy remains; that those patients who were less responsive at baseline, everyone regressed toward the mean, which we know that inflammation does go away when it's related to a short term condition, but the hierarchy of the people that were most responsive and the people that were less responsive remained the same. On the right, you can see the roxadustat-treated patients where they had similar quartiles of responsiveness at baseline due to randomization, but as they were treated with roxadustat, that hierarchy of the blue quartile, being less responsive, no longer remained. Those patients disappeared into the mean of that population, meaning that whatever conferred that

hyporesponsiveness likely was not a factor in

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roxadustat responsiveness.
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             MS. ALIKHAANI: Thank you.
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             DR. LEWIS: Dr. O'Connor?
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             DR. O'CONNOR: I quess I'm back. Chris
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      O'Connor; a question for Dr. Unger. There was a
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     statement (that the boundary of the upper limit of
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     confidence, 0.4, was chosen by the sponsor after
     the blind was broken as 1.3. What would have been
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     your recommendation prior to blind breaking for
     that guidance of the upper limit confidence
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     interval boundary, based on the large number of
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     events in these pooled trials?
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             DR. UNGER: This is Dr. Unger.
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             Thanks, Dr. O'Connor. Well, first of all, I
     wasn't involved in the discussions because this
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     division wasn't within my office at the time.
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     Second of all, we all know that, 1.3, these limits
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     are arbitrary. A 1.3 is reasonable. It was used
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     in the diabetes guidance. It's hard for me to say
     what I might have done, especially now that we have
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     the data in front of us; so it's not a great
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     answer.
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DR. FARRELL: This is Dr. Farrell. I was
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     involved in the negotiations, and after the TREAT
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     trial and dealing with Omontys, we had a goal of
     1.25, and that's what we discussed during meetings.
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     So that's why there was not an agreement on 1.3,
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     and I agree with everything that Dr. Unger has said
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     regarding it's somewhat arbitrary.
             DR. LEWIS: Dr. O'Connor, does that address
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9
     your question?
             DR. O'CONNOR: Yes.
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             DR. LEWIS:
                          Thank you.
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             I will move on to David Soergel.
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             DR. SOERGEL: Thanks. David Soergel. I
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14
     have a question for Dr. Ayache about Study 610.
     And specifically I'm curious about the baseline
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     characteristics in that study that may have
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      contributed to some of the findings that were
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18
      shown, and that might also be a question for the
19
      sponsor.
             DR. FARRELL: Dr. Ayache?
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             What slide, Doctor, would you like to see up
      for 610, or would you rather hear from the sponsor?
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DR. SOERGEL: Let me find it for you. 1 DR. AYACHE: On 610, I will defer this to 2 the sponsor because this study was conducted 3 exclusively in Europe and there was some imbalance 4 between the two arms in baseline and disease 5 characteristics. These balances are not that 6 totally significant, but also I defer it to the 7 sponsor to answer this question in more detail. 8 9 DR. EISNER: Thanks, Dr. Ayache. This is Mark Eisner. I'll ask Dr. Little to 10 speak to the baseline characteristics for 11 Study 610. 12 DR. LITTLE: Yes. Dustin Little. I'd like 13 14 to just remind everybody what Study 610 was. we bring up CO-70 just for a few seconds? 15 Study 610 was the non-alfa study with the 16 active control that's particularly relevant for our 17 18 program because it was not confounded by large differences in treatment discontinuation, and these 19 are the cardiovascular safety results. 20 21 One of the reasons that we thought that this was an important study for us to think about is 22

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because, in many respects, the patient 1 characteristics that drove the differences in 2 treatment discontinuation, the placebo-controlled 3 program, was mostly that being patients having 4 relatively low hemoglobin values and patients 5 having quite low baseline eGFR values were present 6 in this study. 7 So these patients we consider are generally 8 9 representative of the patients in the placebo control trial, and that's one of the reasons why we 10 found it so reassuring that we had the 11 cardiovascular safety results that we had in this 12 study. 13 14 DR. LEWIS: Thank you. I will now turn to our leftover questions 15 for the sponsor from earlier, clarifying questions. 16 Dr. Crowley, do you still have a question? 17 18 DR. CROWLEY: Yes. Thank you. This is for 19 Dr. Little or a representative from FibroGen. In terms of your risk mitigation strategy, I 20 21 was wondering if you had considered inclusion, say, of a moratorium period for people who have had a 22

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recent seizure, or a recent myocardial infarction 1 and a DVT; also in terms of risk mitigation, 2 caution in the use of patients not only who have a 3 history of seizure but have a history of 4 hypercoagulability. I don't know if they were also 5 that cohort of patients who were excluded from the 6 trials as well. 7 DR. EISNER: Mark Eisner here. Thanks for 8 the question. I will refer it to Dr. Little to 9 respond. 10 Dr. Little? 11 DR. LITTLE: Dustin Little. The first part 12 of the question I believe had to do with inclusion 13 criteria, consideration of the types of patients to 14 include in the postmarketing study. We're 15 certainly willing to consider and thinking through 16 some of the details of that study. 17 18 I think probably we would consider taking a 19 similar approach to the approach that we took in the clinical program, where we did not exclude 20 21 patients with a history of thrombosis, but rather patients with a thrombotic event within the last 22

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So I would anticipate that that would be 1 12 weeks. an approach that we would strongly consider. 2 DR. CROWLEY: Then may I also ask you, is 3 there anything that we can learn already from the 4 dosing practices in China and Japan since this 5 medication has been approved already in those 6 countries? Is it typical practice to reduce the 7 doses and to slow the rate of rise of hemoglobin? 8 DR. EISNER: Let me ask Dr. Little to 9 comment at a high level on the safety data. 10 we're talking safety data from China and Japan, I 11 think that will be a lot straighter than -- just to 12 get very specific about dosing practices. 13 14 They are different. The starting doses are a bit different in the two different regions, which 15 does make it a little bit hard to compare apples to 16 apples. For example, the starting doses in China 17 18 are actually slightly higher than they were in the 19 global program. But, Dr. Little, can you just speak at the 20 21 high level about the postmarketing safety data? DR. LITTLE: Yes. Dustin Little. I'd 22

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time.

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actually like to briefly show data that pertains to the question. On the left, we have the number of vascular access thrombosis, deep vein thrombosis, and pulmonary embolism events that have been reported in China and Japan with the reporting rate per 100 patient-years compared to the combined incidence rate from the China and Japan studies. The first thing that I'd like to point out is that in the studies in China and Japan, although they were not as large as those in our pooled program, the rates of thrombosis did appear to be quite a bit lower. It may be that patients in those regions have different risks of thrombosis. Then I'd also like to point out that the reporting rates together between China and Japan are lower than the rates that we saw in the clinical trials in that region. DR. LEWIS: Okay. Dr. Cho, do you still have a question? will say we have a hard stop. We need time to set

up the open public hearing, and it must start on

We have four more minutes, and then we will

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only have a 45-minute lunch. 1 Dr. Cho, do you still have a question for 2 3 the sponsor? DR. CHO: Yes. I have one question. Leslie 4 Cho. 5 Your postmarketing study, in your regular 6 studies for the FDA approval, patients who had MI, 7 it seems that they were excluded for -- if they had 8 it within the year, they were excluded, but your 9 postmarketing study has 12 weeks. 10 Am I confused? Am I wrong? 11 DR. EISNER: Dr. Little, can you please 12 address that question? 13 DR. LITTLE: Dustin Little. The exclusion 14 for myocardial infarction, acute coronary syndrome, 15 and stroke in the clinical studies was within 16 12 weeks prior to randomization. I mentioned that 17 18 that's what we would consider for the postmarketing 19 study, but of course we would plan to discuss the details with FDA. 20 21 DR. LEWIS: Dr. Moliterno, do you have a question for the sponsor remaining? 22

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DR. MOLITERNO: No, Dr. Lewis.
                                               Thank you
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      for asking.
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             DR. LEWIS: Dr. O'Connor, I see you have
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      your hand up. I don't know. Is that for the FDA?
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              (No audible response.)
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             DR. LEWIS: Okay.
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             Dr. Packard, do you have a question? And we
     have three minutes?
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              (No response.)
             DR. LEWIS: Dr. Packer, you may be on mute.
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             DR. PACKER: I'm okay.
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             DR. LEWIS:
                          Okay, great.
             I don't know if you've had a chance to pull
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     up any of the compliance data that I requested or
     you're going to do that after the break and after
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      the open session.
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             DR. EISNER: Dr. Lewis, we'll have that
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     prepared for after the break, after the open
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     session.
             DR. LEWIS: Great. Okay.
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             So we will now break for lunch. We will
      reconvene in approximately 47 minutes at exactly
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2:30 p.m. Panel members, please remember there
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      should be no chatting or discussion of the meeting
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      topic with anyone during the lunch break.
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     Additionally, you should plan to rejoin at about
      2:15 p.m. Eastern Standard Time, 15 minutes prior
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      to the return time, to ensure you are connected
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     before we reconvene at 2:30 p.m. Thank you.
              (Whereupon, at 1:45 p.m., a lunch recess was
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      taken.)
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(2:30 p.m.)

Open Public Hearing

DR. LEWIS: We will now begin the open public hearing session.

Both the FDA and the public believe in a transparent process for information gathering and decision making. To ensure such transparency at the open public hearing session of the advisory committee meeting, FDA believes that it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement to advise the committee of any financial relationship that you may have with the sponsor, its product, and if known, its direct competitors. For example, this financial information may include the sponsor's payment of your travel, lodging, or other expenses in connection with your participation in the meeting.

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Likewise, FDA encourages you, at the beginning of your statement, to advise the committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and this committee place great importance in the open public hearing process. The insights and comments provided can help the agency and this committee in their consideration of the issues before them.

That said, in many instances and for many topics, there will be a variety of opinions. One of our goals for today is for this open public hearing to be conducted in a fair and open way, where every participant is listened to carefully and treated with dignity, courtesy, and respect. Therefore, please speak only when recognized by the chairperson. Thank you for your cooperation.

Speaker number 1, your audio is connected now. Will speaker number 1 begin and introduce

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yourself? Please state your name and any organization you are representing for the record.

DR. KUMAR: First, my name is Jayant Kumar.

I'm a nephrologist with Renal Medicine Associates

in Albuquerque, New Mexico. I am president of the

group and also the program leader for the research

program that is done at our practice.

My conflict for this presentation, it is strictly participating in phase 3 trials with roxadustat. My research site was one of the major sites in the nation for this trial. I have not received any direct honorarium, travel expenses, and I do not own any stock in this company. So with that introduction, I will start my presentation.

Again, thank you for allowing me to speak at this open forum in regards to FibroGen's program of roxadustat for management of anemia in chronic kidney disease and dialysis. As clinicians, management of anemia is one of the paramount comorbidities that we deal with on a daily basis.

Since the advent of erythropoiesis

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stimulating agents like Epogen, Aranesp, Micera, and intravenous iron, the disease state has largely been unattended and the challenge to treating anemia has not been addressed to the maximum.

We all thought that since the availability of ESAs and IV iron, we have found the holy grail, but when multiple randomized-controlled trials were presented that included normal hematocrit study for patients on dialysis, CREATE, CHOIR, and TREAT studies in CKD patients, we found that treating anemia to normal goal, which is a hemoglobin of 13 to 15, was associated with higher risk of cardiovascular mortality, as well as progression of solid tumors.

So FDA inserted a black box warning for the use ESAs. Now, the hemoglobin goal after the KDIGO guideline of 2012 has decreased to 10 to 11 grams per deciliter. While this level may be enough for some people, our patients at this high altitude in New Mexico feel the effects of anemia even at this so-called recommended goal of hemoglobin correction.

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My practice was one of the major sites for phase 3 clinical trials with roxadustat. provide ESRD care to more than 1100 patients in New Mexico and correspondingly a very large number of CKD-4 and CKD-5 populations. Most of our patients live at high altitudes and have multiple comorbidities due to high prevalence of diabetes. This includes a large number of Native Americans and Hispanic patients. As this was an open-label investigation, I could see the response in hemoglobin to roxadustat in our subjects. Roxadustat was able to increase and maintain hemoglobin quite well --DR. LEWIS: Dr. Kumar, your time is up. I'm We have many speakers. I apologize. sorry. DR. KUMAR: Thank you. Speaker number 2, your audio is DR. LEWIS: connected now. Will speaker number 2 begin and introduce yourself? Please state your name and any organization you are representing for the record. MS. BAKER: Hello. My name is Melissia Baker, and I am a 49-year-old proud, fourth

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full-time adoptive mom of a sweet 8-year-old son.

I do not have any financial disclosures regarding
my testimony today.

As a person who has lived with type 1 diabetes for close to 40 years, I became aware of my kidney disease during my early thirties. I received a transplant and fortunately did not need dialysis during my 9-month wait for a new kidney-pancreas.

The seven years with my transplanted kidney-pancreas were wonderful. I resumed a busy life as a Red Cross volunteer and human resources admin and fulfilled my lifelong dream to become a foster parent, which eventually led to my adoption story. But despite heroic efforts by my transplant team, both organs went into rejection seven years after receiving them.

I began life-sustaining hemodialysis

10 years ago while I await a second transplant. I
have a very high antibody count due to my previous
transplant and because of previous blood
transfusions. These factors make another organ

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transplant extremely difficult.

I've suffered from anemia my entire 10 years on dialysis. Even with close monitoring, my anemia can be unpredictable. I have been hospitalized because I needed blood transfusions. Those transfusions are very concerning since they contain additional antibodies. I'm already a highly sensitized transplant candidate. The anemia could make it more complicated for me to receive a second transplant.

In large part, my transplant wait time has been so lengthy due to my highly sensitized status and factors such as anemia. Anemia also makes my chronic fatigue and the low energy levels frustrating. There have been many times when my body simply cannot complete all of the tasks my brain wants to get done.

A treatment for chronic anemia would lessen my worries about future transfusions as it relates to my antigens, and a greater quality of life would help me feel more confident that I could take care of my son and be ready for transplant when the

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opportunity to receive one finally comes. 1 I remain hopeful for a healthier future. 2 The product you are reviewing today could be part 3 4 of that hope for me and so many others like me. ask you to consider that as you make your decision 5 Thank you. today. 6 DR. LEWIS: 7 Thank you. Speaker number 3, your audio is connected 8 9 Will speaker number 3 begin and introduce yourself? Please state your name and any 10 organization you are representing for the record. 11 12 MR. CARR: Hi. My name is Wyatt Carr, Sabin Wyatt Carr. I am 76 years old and I live with my 13 14 wife, Debra [ph], in California. I'm in late stage 4 CKD. I am not a statistic. I am a CKD 15 patient with seven years of real experience with 16 roxadustat. My story is like many people who 17 18 discovered they have CKD. 19 In January 2010, my cardiologist noted a trend in my red blood cell count and thought I 20 21 might have leukemia or blood cancer. He asked if I'd ever had my kidneys tested and ordered a 22

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24-hour GFR test. The test disclosed I was already in stage 3 kidney disease and had anemia.

According to the National Kidney Foundation,

1 in 10 of us will contract CKD and many will

discover their illness the same way I did. As a

non-dialysis CKD patient with anemia, I have been

on and off roxadustat three separate times.

First, FG-4592-041, a trial that began

August 2011 and ended on December 2011; second

FG-4592-059, a long-term trial that began on

May 30, 2012 and ended February 27, 2019 when I was
taken off due to low platelets; and third, this

April I was approved for compassionate use by the

FDA.

While I was on the drug, all the side effects were beneficial, including slowing the decline in my kidney function; more energy; lower blood pressure; improved eGFR readings; higher hemoglobin; less supplemental iron; and improved effectiveness of my statin. These improvements over the past seven years while taking roxadustat allowed me to continue to work, play golf, take

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walks, exercise, attend conferences, and visit companies as part of my work.

After being off of roxadustat since February 2019, I've had to have a blood transfusion in April due to severe anemia. I went from a meaningful quality of life to one where just walking from my bedroom to the living room exhausted me. My hemoglobin dropped to as low as 7.2; GFR as low as 18. I took long naps, lay on the couch most days, and was unable to do things I'd been able to do while taking roxadustat.

Due to my body's issues with inflammation, my doctors and I were concerned that I would likely be a hyporesponder to ESAs. We felt that roxadustat offered the best and possibly the only alternative. Thanks to my doctors at Kaiser, and the IRB, and the FDA, I was permitted back on roxadustat for compassionate use this March.

Again, roxadustat is having beneficial effects. All my subsequent blood tests have shown improvement. I'm extremely grateful to the doctors who helped me get access to this drug through the

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FDA's compassionate use program. I feel like it's 1 given me my life back. There are many others like 2 me who need your help from this awful chronic 3 disease. 4 Thank you, speaker number 3. 5 DR. LEWIS: MR. CARR: I beg of you to consider those 6 7 patients. Thank you. DR. LEWIS: Speaker number 4, your audio is 8 Will speaker number 4 begin and 9 connected now. 10 introduce yourself? Please state your name and any organization you are representing for the record. 11 DR. SILVA: Good afternoon. I am Dr. Arnold 12 I'm a nephrologist and director of clinical 13 research at Boise Kidney and Hypertension Institute 14 in Boise, Idaho in conjunction with Frenova Renal 15 I have served as a clinical investigator Research. 16 on studies evaluating the safety and efficacy of 17 18 roxadustat and I am not financially compensated for 19 my time today. As a physician and clinical investigator who 20 21 has participated in anemia clinical studies with multiple pharmaceutical sponsors for over 20 years, 22

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I am encouraged by both the efficacy of this new oral therapy to treat anemia of chronic kidney disease that has an adverse effect profile comparable to placebo. But I believe roxadustat as an oral agent offers more than a new treatment option to raise hemoglobin in kidney patients with anemia.

In the day-to-day clinical care of patients with renal disease, access to therapy poses difficulties for a patient population that often has socio-economic challenges.

Many rural areas, of which Idaho is an example, pose transportation issues for patients who must travel to medical centers that provide injectable therapies to treat anemia of chronic kidney disease. This impacts patient compliance with treatment and ultimately can adversely affect both their quality of life and clinical outcomes, and oral therapy for anemia can reduce transportation needs and the associated financial burden for many of these patients.

Moreover, in patients with end-stage kidney

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disease on renal replacement therapy, use of oral 1 roxadustat empowers patients to take a more active 2 role in the management of their anemia that can 3 have beneficial effects on both compliance with 4 treatment and their overall well-being. 5 Furthermore, oral therapies can positively impact 6 dialysis workflow in both in-center and home 7 treatment programs, and provide a smoother and more 8 efficient clinical operation. 9 Finally, study data and operations aside, 10 the positive reports from patients taking 11 roxadustat therapy, including stable hemoglobin 12 values with improved energy levels and a preference 13 for oral versus injectable therapies, suggest that 14 roxadustat be given consideration for approval as 15 an additional and important tool to treat anemia 16 chronic kidney disease. 17 18 Thank you for the opportunity to speak 19 today. Your consideration is most appreciated. DR. LEWIS: Thank you, speaker number 4. 20 21 Speaker number 5, your audio is connected Will speaker number 5 begin and introduce 22 now.

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yourself? Please state your name and any 1 organization you are representing for the record. 2 3 MS. LUEBBERS: Hi. My name is Bridget Luebbers. I am a dialysis patient, and I have no 4 financial disclosures to share. Anemia has 5 impacted my life in so many ways. When I was 6 diagnosed with kidney disease 21 years ago, the 7 first step in my treatment was to start medication 8 9 to treat my anemia. Since that day, I have battled to keep my blood levels normal. 10 Being a dialysis patient, I already struggle 11 to find energy just to complete everyday tasks like 12 showering, doing dishes, or even just brushing my 13 teeth, but when my blood count is low, it makes all 14 of these things near impossible. 15 I have had so many ups and downs with my 16 hemoglobin levels that at this point I just know 17 18 when my numbers are low. I can tell because 19 breathing becomes more difficult, walking upstairs feels like climbing a mountain, and I'm forced to 20 21 be still, lay down, and focus on my breathing because it feels like my lungs are never full. 22 My

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limbs become weak, it interrupts my life, and it's a huge inconvenience. I've even ended up at the point when my blood count is so low, and I'm not taking in enough oxygen that I pass out.

One particular instance of this stands out to me. It was in the middle of the night, and I woke up to use the restroom. When I stood up and took my first step, I immediately passed out and fell to the floor. After a minute, I awoke scared and in pain from the fall. The next morning I went straight to the emergency room, and upon triage, they rushed me back to see a doctor. I was as white as a ghost. They knew just from looking at me that I was severely anemic.

That resulted in a multi-day hospital stay and many units of blood transfused just to get me back to a sustainable level. I unfortunately have had many blood transfusions over the years, and as a dialysis patient hoping for a transplant, I knew transfusions were dangerous because in addition to the everyday risks of a transfusion, when you want a kidney transplant, you could end up building

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antibodies from the transfusion which would make it 1 more difficult to find a kidney match. 2 So over the past 21 years, I've had multiple 3 medications to treat my anemia and have ridden the 4 roller coaster of ups and downs with my levels 5 getting too high or dropping too low, having a hard 6 time finding a balance. 7 Having a new treatment like this will be so 8 9 helpful because many people are like me and battling this rollercoaster ride of ups and downs. 10 We always try to stay positive, we try to keep on 11 12 with our regular lives, and we try to do the best we can to be normal. But it's hard to do that when 13 14 exhaustion is your constant companion. I ask that you remember this as you consider 15 your decision today. All of our bodies are 16 different, and as more medications become 17 18 available, more people in my situation will find 19 some peace in their life as they can find the right medication for them. Thank you for your time. 20 21 (Pause.) DR. YU: Dr. Lewis, are you there? 22

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Speaker number 6, your audio is DR. LEWIS: Will speaker number 6 begin and connected now. Please state your name and any introduce yourself? organization you are representing for the record. DR. PAUL: My name is Dr. Subir Paul. have been a practicing nephrologist in northwest Alabama, in Shoals Kidney and Hypertension Clinic in Florence, Alabama for the last 25 years. I'm a fellow of the American Society of Nephrology. also trained resident physicians, medical students, and do clinical trials. I was one of the principal investigators of the phase 3 trial and have no financial disclosures relevant to the product of roxadustat and today's talk. I am speaking on my own behalf. For last three decades, we have been treating anemia of CKD with various erythropoiesis stimulating agents, or ESA, and IV iron. intestinal iron absorption is poor in our patients, when inflammation develops in many of our CKD patients, hepcidin expression in liver goes up, preventing iron absorption and iron mobilization;

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thus erythropoiesis goes down causing ESA resistance.

I became interested to be a principal investigator for this trial for a number of reasons. Number one, it is a novel oral agent.

Number two, it has a unique mechanism of action.

It inhibits hypoxia inducible factor prolyl hydroxylase, and this stabilizes HIF and increases endogenous erythropoietin production.

Number three, it inhibits hepcidin and increases iron absorption and iron transport to bone marrow for erythropoiesis. Number four, I felt that this approach is physiological and this agent will be effective and safe.

I found that the patients who are treated with roxadustat have a [indiscernible] significant rise of hemoglobin without much need for IV iron. They felt significantly better. Their energy level improved, shortness of breath decreased, and they were highly satisfied. It offers a very similar advantage for patients on peritoneal dialysis and for patients with CKD not on dialysis who live 56

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to 70 miles away from my office or from the 1 dialysis center. Many are elderly who cannot drive 2 and face problems in getting transportation. 3 Thus, CKD anemia patients not on dialysis 4 while receiving ESA need frequent IV iron therapy 5 with the vein punctures. These repeated injuries 6 to the veins may cause significant issues for good 7 fistula formation and fistula functioning and 8 increase the risk for total [indiscernible] 9 catheter placement for hemodialysis. Total 10 [indiscernible] catheter increases the risk for 11 blood stem infections and mortality. 12 I have seen ESA resistance in many of my 13 14 patients and this probably will be of significant benefit to them. If approved by FDA, roxadustat 15 will be beneficial to treat anemia in patients on 16 maintenance hemodialysis, peritoneal dialysis, and 17 18 CKD patients not on dialysis. It will be 19 especially very useful --20

DR. LEWIS: Thank you, speaker number 6. Your time is up.

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DR. PAUL: Thank you for your attention.

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Speaker number 7, your audio is DR. LEWIS: Will speaker number 7 begin and connected now. Please state your name and any introduce yourself? organization you are representing for the record. My name is Dr. Jessica DR. COLEMAN: Hi. Coleman. I'm a private practice nephrologist with Nephrology and Hypertension Medical Associates. have a financial relationship with AstraZeneca through my position as a paid speaking consultant, and that's my only disclosure. With that, I'm going to go ahead and start my three minutes. I want to first thank the committee for this opportunity to share not only my experience, but my patients' experience with anemia of CKD and give some clinical insight into the burden of this disease state. We know that anemia in CKD is prevalent with 5 million adults in the United States suffering from the disease, but less than 25 percent of patients provided care prior to dialysis initiation. I'd like to give you a clinical vignette that highlights why this occurs and possibly why

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having an oral agent would really be very 1 beneficial to treat this disease state, and I 2 really believe an oral agent would revolutionize 3 the field. I don't need to go into the common 4 symptoms of anemia. The previous speakers, and 5 especially the patients, have done an eloquent job 6 of sharing how it impacted their personal lives. 7 But as clinicians, we know there are even more dire 8 9 potential outcomes. The subclinical symptoms of fatigue and 10 dizziness can have end-organ damage, hypoxic 11 12 injury, so that there's a really substantial impairment that occurs to the patient and to their 13 disease process. Current guideline-directed 14 therapy can be very difficult to achieve, so I'd 15 like to talk about a very typical patient in my 16 clinical practice, Ms. A. 17 18 She is a 62-year-old African American female 19 who has stage 3B CKD with a GFR of 32 percent, diabetes, hypertension, cardiac disease, and she's 20 21 a caregiver for her elderly mother and uncle, as well as two young great-grandchildren. Her average 22

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hemoglobin is 9.8 over the last three years that I have cared for her. She routinely feels tired, run-down, and in order to treat her anemia, we have sent her to hematology so that she can receive IV iron, ESAs, and other supplemental strategies as appropriate. However, she lives over an hour away; therefore, to come every other week to receive her injection, or not if her hemoglobin is too high, she has to arrange care for four other individuals. She has to align transportation at least 3 days prior to her appointment, and has an average of a 5-to-6-hour day just for receiving simple ESA injection, and that's assuming everything goes well with no delays. There's also a financial burden

Ms. A therefore understandably has trouble appreciating her obvious time commitment, logistical difficulties, and financial burden, and whether or not that's actually worthwhile. What she doesn't understand is that by missing

which costs an average of \$40 transportation one

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appointments and not participating fully in our own 1 health care, she's actually working against 2 herself, and thereby perpetuating the vicious cycle 3 of anemia in CKD. 4 Currently today in my office, I'm seeing 5 28 patients, 15 of whom have anemia of CKD and have 6 7 similar appearances and challenges to Ms. A. She's --8 9 DR. LEWIS: Thank you, speaker number 7. Speaker number 8, your audio is connected 10 Will speaker number 8 begin and introduce 11 12 yourself? Please state your name and any organization you are representing for the record. 13 DR. WEI: Good afternoon. Dr. Alice Wei 14 speaking. I have been a nephrologist in private 15 practice in Harlem of New York City for over 16 I've no financial disclosures to make, 17 18 and I'm speaking on behalf of myself and patients. 19 Many inner-city groups, including patients like mine in Harlem, have difficulty accessing 20 21 medical care. Either because of frailty, health literacy, or health system inefficiencies, most 22

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patients are unable to obtain the standard treatment for severe anemia of chronic kidney disease. Patients are afraid to inject themselves with ESAs. They find going to a doctor's office every week or month for injections taxing, and some patients who need to be referred to a hematologist or hospital setting for IV iron infusion find this too burdensome.

Anemia of CKD leads to many of the symptoms we associate with frailty as we heard from patient speakers earlier: easy fatigability, weakness, slowness of gait, and diminished cognition. It also increases the risk of CKD progression, cardiovascular morbidity, and mortality.

Since ESA trials have not shown to improve mortality or other hard outcomes, we are desperate for another option to treat anemia of CKD. Because roxadustat is an oral medication, it will be far more accessible to patients in need, and because roxadustat also enhances iron absorption from the gut, we can expect less need for IV iron infusions.

Improvement in anemia means less

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transfusions, too, which leads to a better chance 1 of patients having a successful kidney transplant. 2 This will ultimately offer a better patient 3 experience, better outcomes, and less utilization 4 of services such as physician office visits, 5 injectable or infusion medications, and 6 transfusions. 7 With an option like roxadustat, I can be 8 assured my patients can get the treatment they 9 need, so I spend less time coordinating expensive 10 services and more time treating patients, focusing 11 on maintaining their kidney health and keeping 12 patients off dialysis. 13 14 Thank you for your time and your consideration in approving roxadustat as a new 15 treatment option for anemia of chronic kidney 16 disease. 17 18 DR. LEWIS: Thank you, speaker number 8. 19 Speaking number 9, your audio is connected Will speaker number 9 begin and introduce 20 21 yourself? Please state your name and any organization you are representing for the record. 22

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DR. MANLLO-KARIM: Good afternoon. My name is Roberto Manllo-Karim. I am a nephrologist in a group practice in south Texas with eight additional partners. We care for roughly 1,300 dialysis patients and over 5,000 patients with CKD. I have been practicing nephrology for almost 30 years. Conflict of interest, I participated as principal investigator in clinical trials for FibroGen. own 1000 shares of FibroGen stock. I didn't receive any underwriting for this presentation. I don't think I have to educate the community regarding the high prevalence of anemia in chronic kidney disease, especially stages 4 and 5. Anemia not only causes multiple symptoms but also has an impact on cardiovascular events, progression of chronic kidney disease, and overall mortality. One thing that practicing physicians like myself know is the level of therapeutic inertia that occurs given the limited choices available to us to treat anemia. Basically, we have three options: iron supplementation, erythropoietin

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stimulating agents, and transfusion. 1 We all know about issues of tolerability of 2 oral iron supplementation. There are even higher 3 risks when it comes to intravenous iron 4 supplementation, including hypertension, allergy, 5 and the inability to use in the setting of 6 infections. 7 Erythropoietin stimulating agents carry the 8 9 risk of hypertension, stroke, progression of 10 malignancy, as well as graft thrombosis. Transfusion is out of favor due to possible 11 allosensitization of future transplant recipients. 12 What my patients and I like about the use of 13 roxadustat is that it mimics normal adaptation to 14 altitude. This is basic physiology as opposed to 15 supratherapeutic doses of ESAs and very high doses 16 of intravenous iron supplementation, which no human 17 18 being ever sees in their lifetime under normal conditions. 19 We all know well about the role of 20 21 functional iron deficiency in chronic kidney disease that limits iron availability. Roxadustat 22

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allows not only physiological rising EPO levels but also enhances oral iron absorption. We frequently encounter dialysis patients with anemia that have a high ferritin but a low iron separation. afraid to give a patient additional intravenous iron because of the high ferritin, but at the same time they may not respond to erythropoietin because of the low iron separation. HIF inhibitors such as roxadustat will allow additional iron availability and increase EPO levels. Roxadustat will be a great agent of choice for these types of patients. In my experience, roxadustat is well tolerated, safe, and effective, and should become first-line treatment for anemia in patients with chronic kidney disease in the office. It should also be an option for treating anemia in dialysis patients, especially peritoneal dialysis, rivaling [ph] the time-tested erythropoietin. Thank you very much for your attention. DR. LEWIS: Thank you, speaker number 9. Speaker number 10, your audio is connected

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Will speaker number 10 begin and introduce 1 yourself? Please state your name and any 2 organization you are representing for the record. 3 MS. DILGER: Hello. My name is Amanda 4 Dilger and I'm speaking on behalf of my dad, Eugene 5 Miller. This letter is to explain how his 6 diagnosis has affected both his and my family's 7 lives. We have no financial disclosures. 8 My dad is 67, has two kids and three 9 10 grandchildren, and currently lives with my family. He worked as a self-employed truck driver for over 11 40 years. He enjoys the simple things in life like 12 farming, listening to music, and talking with 13 friends and strangers alike. He has a generous 14 heart and an inquisitive personality. 15 When he was diagnosed, we didn't quite 16 understand the ripple effects it would have on our 17 18 With long hospital stays, long ER visits 19 for blood, and coordinating his care, quality of life has dramatically changed. Before CKD, he was 20 21 independent and managed his own daily needs. He was healthy and enjoying his retirement. 22

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My dad's CKD was triggered after a MRSA infection that affected multiple joints. Unexpectedly, he became handicapped and unable to walk or use his right hand. He had to move in with As a result, we built ramps for him to better access our home, but now that limits how we can park in our garage. To get him anywhere, we must maneuver vehicles around for him to get down the ramp, move around the vehicle, and we lift the heavy equipment in and out of the vehicle for appointments. It most reminds me of when I would struggle to get my stroller through the door at the mall that wasn't automatic; one child in the stroller, one holding my hand, and my foot trying to pry the Physically, the in and out of the car door open. for appointments can be incredibly painful and occasionally seems impossible. He's always willing his body to cooperate, and I can only watch as he

Fifteen feet into the infusion building with manual doors can be quite the trek for us. In the

struggles to transfer.

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early days when we were both learning, he may have 1 accidentally rolled away from me a few times as I 2 was trying to hold the door and wheel him into the 3 building at the same time. We laugh about it. 4 Getting him to his injection appointments 5 isn't just a strain on us physically but 6 logistically as well. As a family of five plus my 7 dad, we have a very busy schedule. This is just 8 9 the smallest glimpse into our struggles of getting him to injections outside of our home. 10 There's no doubt in my mind that having an 11 oral treatment like roxadustat would be 12 life-changing and reduce some of the physical 13 difficulties of in-office treatment. Thank you for 14 your time. 15 Thank you, speaker number 10. DR. LEWIS: 16 Speaker number 11, your audio is connected 17 18 Will speaker number 11 begin and introduce 19 yourself? Please state your name and any organization you are representing for the record. 20 21 MS. GRIFFITH: Hi. My name is Elizabeth Griffith. I am 49 years old. I have no financial 22

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disclosures.

When I was in grade school, I was told I had anemia due to kidney disease due to a birth defect. Up till 2016, I was able to work, go to school, and do anything I wished without thinking about it, but my life has drastically changed since 2016. I have been unable to work due to now having ESRD and being very anemic.

My nurse has been at a wits end trying over the years to get my hemo levels constant. Previous medication would raise my levels for a day or two, and then it would crash. I was getting the highest dose possible and nothing was helping.

I learned about the trial for this drug from my nurse and doctor. I was so grateful for something that could help me get my energy back and even to do the simple things that most people with normal amounts of energy take for granted, just going to the market, visiting friends, or household chores.

I started the trial in November 2020. Since then, I've gotten my energy back and my life back.

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I've been able to schedule daily activities. the small things like making taco sauce, dinner, or even getting the dishes done I've been able to do without taking a break and completing the task That is something that I haven't been able fully. to do since 2016. I'm sharing my story with you because I hope it makes you understand just how much someone struggles with anemia because of kidney disease, the exhaustion that steals the normal things from us year after year. Please consider me as you make your decision for this drug. Thank you so much for the chance to speak. Have a great day. DR. LEWIS: Thank you, speaker number 11. Speaker number 12 is not going to speak. Speaker number 13, your audio is connected Will speaker number 13 begin and introduce yourself? Please state your name and any organization you are representing for the record. MR. CRUMBAUGH: Hello. My name is Louard Crumbaugh, Jr., and I am an 82-year-old retired nuclear engineer now living in Nampa Idaho since

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returning to the U.S. from living and working in Israel for three years. About six years of being back into the country, my doctor explained to me that because of my high blood pressure, my kidneys were failing. Using diet and medications to try to control my high blood pressure was not successful in my case.

My kidney function continued to decline until about two years ago when I was told that I was in complete kidney failure. One of the major problems that I had was anemia. The doctor and I tried to control it with iron supplements with limited success. The next step was to give me iron through infusion.

Getting the infusions worked great but had a few drawbacks. About every 3 to 4 weeks, I had to go to the infusion unit at our local hospital for my injection. First, a sample of my blood was taken and sent to the lab to determine my hemo level, and then after the lab sent the results back to the infusion unit nurse, she would then send an order to the hospital pharmacist to make up the

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required amount of medication for the infusion. And depending on the workload that the nurses had in the infusion unit, some days I was maybe in the infusion chair for 3 hours or better. This is unusual I think. Taking my blood samples to check for my hemo levels does not sound like anything abnormal, but for me, because of my small veins, most of the nurses had a very difficult time trying to get a sample from me. Many times I'd have large bruise spots on my arms where the nurse had to stick me 3 or 4 times in an area trying to hit a vein with no luck; then after 3 weeks when the bruises were almost healed, it was time for my next iron infusion. During a visit to my dialysis clinic, I was informed about this trial research of a product which would eliminate getting iron infusions. Would I be interested in participating? Oh boy, would I? Here was a product that would help me maintain my hemo levels without these monthly blood draw and iron injections. For me, I feel that the results of taking 1

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or 2 pills 3 times a week to give me the same, if 1 not better, results of the iron injections that I 2 took was a real plus. The cost savings alone would 3 be a big selling point. No nurse needed to draw my 4 blood, as well as no lab work needed. The hemo 5 levels could be checked during my regular routine 6 blood work. The hours spent sitting in the 7 infusion chair, now I could utilize it doing 8 9 something at home, reducing the size of my honey-do list. 10 DR. LEWIS: Thank you, speaker number 13. 11 Your time is up. 12 Speaker number 14, your audio is connected 13 14 Will speaker number 14 begin and introduce yourself? Please state your name and any 15 organization you are representing for the record. 16 DR. RASTOGI: Thank you very much. 17 My name 18 is Anjay Rastogi. I'm professor of medicine and 19 clinical chief of nephrology at UCLA Health. not being paid for speaking today, but I've been 20 21 heavily involved with CKD anemia research for the past decade and a half, and I've served as a PI on 22

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several HIF stabilizer studies, including those conducted by FibroGen, AstraZeneca, and GSK. also on the Speakers Bureau for AstraZeneca and also act as a consultant for them as well. Anemia of CKD is quite prevalent in the U.S., presenting a significant disease burden with roughly 5 million patients affected, and quite a few of them not being treated for multiple reasons, including access to care and also the fact that most of the drugs that we're using are injectables. Anemia of CKD also has a significant impact on quality of life and is associated with significant morbidity and mortality. All the testimonials that we have had from

All the testimonials that we have had from our patient colleagues, I would completely agree with that; that is my patients say exactly the same things as well.

Prior to recombinant erythropoietin's launch in 1989, a blood transfusion was the main way anemia of CKD was managed. Blood transfusion is something we want to avoid, especially in patients with CKD for the risk of alloimmunization, which

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can complicate the chances of transplantation in the future. Recombinant erythropoietin was very successful in doing this, however, we soon found out that there were significant potential risks associated with recombinant erythropoietin, including mortality, for which it received a boxed warning in 2007.

At the same time these things were happening with recombinant erythropoietin, there were significant advances being made in our understanding of anemia CKD, especially the HIF pathway, and a Nobel Prize was given out in 2019 in medicine or physiology for this.

HIF stabilizers, or hypoxia-inducible factor stabilizers, work more upstream than recombinant erythropoietin and lead to a more coordinated approach to anemia of CKD management, including utilizing endogenous Epogen and more optimal utilization of iron.

Another advantage of HIF stabilizers is that they're oral. This is of special benefit in non-dialysis-dependent CKD patients and home

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dialysis. A couple of things to keep in mind that 1 were not discussed so far was passing of the 2 American Advancing Kidney Health Initiative in 3 4 2019, with a major focus on increasing home dialysis and transplantation. 5 We also need to keep the COVID-19 pandemic 6 in perspective. Our hope is that these oral agents 7 will really push more transplantation and more home 8 dialysis and at the same time keeping our patients 9 10 safe at home. I want to again thank you for having me participate. 11 12 DR. LEWIS: Thank you, speaker number 14. Speaker number 15, your audio is connected 13 14 Will speaker number 15 begin and introduce yourself? Please state your name and any 15 organization you are representing for the record. 16 MS. WILLIAMS: Hello, everyone. My name is 17 18 Leigh-Ann Williams. I live in Monroe, Louisiana, 19 which is right outside New Orleans, and I'm the Ambassador for the American Kidney Fund. I thank 20 21 you all for giving me the opportunity to talk about living with kidney disease and anemia. 22

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I have a bachelors in toxicology from the University of Louisiana Monroe, a masters of science in clinical toxicology from the University of Florida, and a master of public health from LSU Health Sciences Center in New Orleans, and I currently work in the healthcare field. So I have plenty of education and experience, but none of this has shielded me from anemia. Given that I am used to hemodialysis and needles, the extra stick each month for an additional iron series doesn't bother me. The part of anemia that I find most difficult is the constant lethargy, which is coupled with being tired and worn out from work and dialysis. It is really challenging every day to get up

It is really challenging every day to get up and do daily activities, even simple things around the house. You can manage to do a few little things, but you'll be tired from exerting even just a little bit of energy.

The constant feeling of never getting enough rest truly takes a toll on you. Even if I somehow manage to sleep for 10 uninterrupted hours, I would

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still get up and feel sluggish like I did not get enough rest, and this struggle is just to do a little bit of chores around the house.

It is hard to get up at a good time to go to work because you're always tired and sluggish. I even at one time needed to get several blood transfusions to increase my hemoglobin in my blood. Additionally, day in and day out, you're always cold. You always have to have something extra with you, even a jacket because you'll feel uncomfortably cold in neutral or regular temperatures. You can eventually feel warm enough, but this is just another example of why living with anemia is so difficult and so draining.

For us anemia patients, we need options.

Everything doesn't work for everyone, so we need as many available treatments as possible. There is no one fix for all. Thank you very much for your time today, and I sincerely appreciate the opportunity to share my story about the struggles of living with kidney disease and anemia.

DR. LEWIS: The open public hearing portion

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of this meeting has now concluded and we will no
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     longer take comments from the audience.
2
                      Dr. Lewis, hi. I'm so sorry.
3
     is Joyce. We have one more speaker, number 16.
4
             DR. LEWIS: Oh, number 16 did come. Okay,
5
             I apologize.
     great.
6
             Speaker number 16, your audio is connected
7
           Will speaker number 16 begin and introduce
8
     yourself? Please state your name and any
     organization you are representing for the record.
10
             MR. SPIGLER: Good afternoon. My name is
11
     Mike Spigler, and I'm the vice president of patient
12
     services [indiscernible - audio feedback] for the
13
     American Kidney Fund. I do not have a personal
14
     financial relationship with the applicant.
15
             [Inaudible - audio feedback].
16
             So on behalf of the American Kidney Fund,
17
18
     and myself as a primary caregiver to a kidney
19
     disease patient with anemia, I want to thank you
     for the opportunity to address you.
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21
             Anemia is very common in people with chronic
     kidney disease, also known as CKD. CKD patients
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with anemia often struggle with quality of life 1 [inaudible - audio feedback] -- just like my 2 mom -- [inaudible]. 3 [Inaudible]. However, over the past 5 to 10 4 years we've seen many innovations in rare kidney 5 disease, [inaudible] -- innovative treatments in 6 CKD-related anemia. And while current anemia 7 treatments have been an important part of effective 8 CKD management, there is room for improvement. 9 As COVID-19 [inaudible] -- need greater 10 ability to manage their own care. This is 11 especially true for two groups of patients 12 [inaudible] -- and those who are doing dialysis at 13 14 home. While some patients can be taught to self administer injections at home, it is not for every 15 patient. 16 [Inaudible] -- severe economic hardships, 17 18 and at the American Kidney fund, transportation is 19 the most common request for financial assistance from our safety net program. Providing anemia 20 21 treatment options for patients that will offer less travel to and from a provider for an injection 22

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would be welcomed by many of the patients.

I want to thank you again for allowing the American Kidney Fund and some of the patients and [inaudible].

Clarifying Questions (continued)

DR. LEWIS: Thank you, speaker 16, and thank you, Joyce.

The open public hearing portion of this meeting has now concluded and we will no longer take comments from the audience. We will now take remaining clarifying questions for all the presenters thus far.

Please use the raised-hand icon to indicate that you have a question and remember to put your hand down after you have asked your question.

Please remember to state your name for the record before you speak and direct your question to a specific presenter, if you can. If you wish for a specific slide to be displayed, please let us know the slide number, if possible.

As a gentle reminder, it would be helpful to acknowledge the end of your question with a thank

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you and the end of your follow-up question with,
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      "That is all for my question," so we can move on to
2
      the next panel member.
3
             Dr. Packer?
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             DR. PACKER: Yes. Thank you so much.
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             I just want to give the sponsor a chance to
6
7
      address the point that I raised earlier about
     all-cause mortality. It's really the one safety
8
      issue I want to ask about.
9
             Can the sponsor show slide CO-78, please?
10
             Now, I just want to make sure; this is the
11
     only slide I think the sponsor showed on all-cause
12
     mortality in the DD trials. Now, this excludes
13
     trial 613.
14
             I just want to call everyone's attention to
15
      the fact that there are 1940 patients in each
16
      treatment group, and altogether there are about
17
18
      439 deaths. You can see the hazard ratio for
19
      all-cause mortality, which is not statistically
      significant.
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21
             Can I have the sponsor go to figure 68 in
      their briefing document?
22
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DR. EISNER: Yes, Dr. Packer. It's Mark 1 We'll work on pulling that up, and 2 Dr. Little will be addressing this question. 3 DR. PACKER: Okay. This comes from the 4 sponsor's briefing document. It's exactly the same 5 set of trials. It's the DD trials, all three 6 7 DD trials, excluding 613. It shows all-cause mortality, again. 8 9 Let me point out the denominators are the 10 same, 1940 in each group. Here we have all-cause mortality and we have 782 deaths. Now, the hazard 11 12 ratio here is 1.17. It goes from 1.02 to 1.35. Now, there are 350 more deaths in this analysis 13 14 than in the slide that the sponsor showed to the committee. 15 Can I go back to slide CO-78? This is the 16 slide you showed the committee. Is it correct to 17 18 say that this isn't an analysis of all-cause 19 mortality; this is an analysis of mortality as the first event in MACE? Is that correct? 20 21 DR. EISNER: I'll ask Dr. Little to address 22 your question.

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(No response.) 1 DR. EISNER: Dr. Little, you may be on mute. 2 I'm sorry for the delay. 3 DR. LITTLE: is Dustin Little. 4 Dr. Packer, what's reported is all-cause 5 mortality. All deaths are analyzed that occur in 6 the OT-plus-7 days analysis window. 7 DR. PACKER: That can't be true. Go back to 8 your previous slide. Go back to figure 68. 9 are 782 deaths here in the same three trials. 10 Now go back to the slide you just showed me. 11 There are 439 deaths. This is not an analysis of 12 all-cause mortality; this is an analysis of deaths 13 14 that occurred as the first event in your MACE analysis. 15 Isn't that correct? 16 DR. LITTLE: Dr. Packer, what we're seeing 17 18 on the screen is the results for on-treatment-19 plus-7 days analysis set. Then the figure that you're referring to from the briefing document, 20 21 that's the so-called ITT or the on-study analysis. I'd like to just take a minute to address 22

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that, if I may. Could we please go to CO-74?

Let's take another look at the disposition of patients. One of the challenges of the on-study analysis is that there are some patients with missing information.

If we can quickly go to CO-75, the FDA in their presentation, they mentioned that one of the limitations of on-study analysis can be the inclusion of rescue therapy or alternative therapies following discontinuation of the interventional treatment, and that certainly would be expected to be the case with roxadustat.

I showed you on the previous slide that we do have some missing data in our ITT analysis for all-cause mortality. One of the three studies has more complete follow-up with actually 99 percent ascertainment of MACE. That's Study 002, and that study has a hazard ratio point estimate for all-cause mortality of 1.09, which is more consistent with the overall results.

DR. PACKER: I'm sorry. Please forgive me. You're not answering my question.

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Can we just go back to your figure 68 in 1 your own briefing? 2 Dr. Packer, it's Mark Eisner 3 DR. EISNER: I think the difference is in the 4 again. ascertainment window. OT-7 is a much shorter 5 ascertainment window than on-study, where patients 6 are followed off treatment to the end of the study; 7 so more deaths are captured because they're 8 followed for longer during that ascertainment 9 window. 10 So I think the discrepancy that you're 11 focusing on is not really a discrepancy. It's just 12 a difference between an OT-7 ascertainment window 13 14 and an on-study ascertainment window, which could have followed patients for much, much longer. 15 Does that help? 16 DR. PACKER: It does help, and I appreciate 17 18 the clarification very much. But can I maybe just 19 ask one more thing? You're showing a similar effect may be a 20 21 slightly greater risk with your agent compared to an ESA, which is labeled for an increase in 22

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mortality.
1
             Now, can you put up the mortality data for
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      the Study 613?
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             DR. EISNER: We will do. And while we're
     pulling it up, let me just say that the ESA doses
5
     we used in our pivotal trials were lower than those
6
     that were used in other studies such as the normal
7
     hematocrit study or CHOIR. And what you can see on
8
     the bars on the right is our epoetin alfa dosing
9
      level versus those that are used --
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             DR. PACKER: I understand that, but can you
11
     put up the all-cause mortality for Study 613?
12
             DR. EISNER: Yes, we're working on that. I
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14
     was just trying to clarify the epoetin alfa risk in
      our trials is actually lower than the --
15
              (Crosstalk.)
16
             DR. PACKER: It may be, but --
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             DR. LEWIS: Dr. Eisner, can we put up the
19
      slide he's requesting, please?
             DR. EISNER: Yes, we're working on that.
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21
             DR. LEWIS:
                          It's in your deck.
             DR. PACKER: I just want to say that it
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could be that the epo dose is lower, but we don't
1
     know that the epo dose that you're using is not
2
      associated with an increased risk of death.
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             DR. EISNER: That's a fair point.
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             DR. PACKER: Please, I don't want the
5
     meta-analysis; I want the Kaplan-Meier curves for
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7
     Study 613, all-cause mortality, please.
             DR. EISNER: We will get that for you.
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9
             I believe this is what you're looking for.
             DR. PACKER: Yes. Let me just say that the
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      FDA did an analysis of this. This is a comparison
11
     of roxadustat versus two different ESAs.
12
     not part of the meta-analysis; this is all-cause
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     mortality. I believe the hazard ratio here is
      1.54, with a lower bound that is greater than 1.
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             Is that correct?
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             DR. EISNER: Let me ask Dr. Little to
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18
      address that question and also to speak a little
19
     bit more about the study more generally.
             Dr. Little?
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             DR. LEWIS: Dr. Little, if you could confine
      your comments to answer Dr. Packard's questions
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specifically. 1 DR. LITTLE: Yes. Dustin Little. 2 The hazard ratio point estimate is estimated 3 4 to be 1.67 on our analysis using the study-specific stratification factors with the lower bound of 5 1.12. 6 May I have a moment to show some information 7 on dosing? Just briefly, we talked about how there 8 were some differences between Study 613 and the 9 other trials, and one of the differences was that 10 higher starting doses of roxadustat were used in 11 Study 613. 12 Just on the left, we have a few metrics 13 14 suggesting that starting doses may have been too high, and we note that in the DD pool -- that's the 15 three studies -- dose reduction, dose holds, 16 hemoglobin overshoots, and rapid rates of 17 18 hemoglobin rise were more common for roxadustat 19 versus epoetin alfa, but that was particularly more common in Study 613. This is one of the design 20 21 differences in Study 613, which --DR. PACKER: I really appreciate that. 22

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Thank you very much. 1 Are you implying that there is a 2 dose-dependent increase in mortality with 3 roxadustat? I think you just said that, right? 4 DR. EISNER: Dr. Little, would you like to 5 address the question? 6 DR. PACKER: You said that you used higher 7 doses and you got a hazard ratio of 1.54. You used 8 lower doses; you got a hazard ratio of -- well, it 9 sort of depends on which one you look at it. 10 Is that what you're telling us? I think 11 that what you just said. 12 DR. LITTLE: Dr. Packer, when we look at our 13 data to investigate for dose-dependence regarding 14 all-cause mortality in MACE, we don't find it to be 15 particularly conclusive. So our mitigation 16 strategy regarding our dosing really is aimed at 17 18 thrombosis. 19 I think some people would consider that the mitigations that have been undertaken with ESA, and 20 21 we're undertaking similar mitigations with roxadustat, have been aimed at reducing 22

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cardiovascular risk. But the most clear evidence 1 that we can provide is that we accept our dosing 2 changes to mitigate risk of thrombosis. 3 We do consider that, overall, when we look 4 at our data versus ESA in the dialysis population, 5 including when we pooled Study 613 with the other 6 studies, that we don't see evidence of increased 7 cardiovascular risk with roxadustat versus ESA. 8 9 DR. LEWIS: Thank you, Dr. Packer, and thank you, Dr. Little. 10 Can we go on to the compliance data? 11 DR. EISNER: Yes, I'd be happy to show you 12 that. 13 14 DR. LEWIS: Also, Dr. Eisner, if you have how often there were dose adjustments made in the 15 roxadustat group, I would like to see that data as 16 well. And we have two more questions, maybe three 17 18 now, so we'll move quickly to direct answers 19 specifically. DR. EISNER: Okay. I'll ask Dr. Szczech to 20 21 address your question about compliance. Dr. Szczech? 22

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DR. SZCZECH: Thank you very much. We used
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      the protocol-specified definitions of how we would
2
      analyze compliance at greater than 75 percent to
3
     pull this side together. As you can see in the NDD
4
     population, we had 95 to 99 percent compliance
5
     based on each study in the NDD population, and --
6
                          Thank you. It's easily read and
7
             DR. LEWIS:
      answers that part of my question.
8
             Is there any correlation, or did you see any
9
     correlation, between non-compliance and adverse
10
      events, or hemoglobin being out of range or rising
11
12
      too quickly?
             DR. SZCZECH: No, we did not see any
13
14
      evidence of that.
             DR. LEWIS: You didn't see it or you didn't
15
     do the analysis?
16
             DR. SZCZECH: We didn't see it.
17
18
             DR. LEWIS: So you have an analysis to
19
      show --
             DR. SZCZECH: I don't have an analysis --
20
21
             DR. LEWIS: -- that noncompliance didn't
      affect that?
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DR. SZCZECH: I don't have an analysis to
1
      show you via slide. We can try to get you that
2
      information.
3
4
             DR. LEWIS:
                          Thank you.
             DR. SZCZECH: But there --
5
             DR. LEWIS: Sorry?
6
             DR. SZCZECH: I'm done.
7
                                       Thank you.
             DR. LEWIS: Ms. Alikhaani, you have a
8
9
      question.
10
              (No response.)
             DR. LEWIS: I think you're muted still.
11
             MS. ALIKHAANI: This is Jacqueline
12
     Alikhaani. I'm very concerned about the safety
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14
      issues presented by the FDA and I agree with those.
      They seem very reasonable to me, and it seems like
15
      it should be possible to better address and remedy
16
      those safety concerns and risk factors for
17
      roxadustat.
18
19
             I just want to know to the sponsor, I just
     have this question. Are you willing and able to
20
21
     work to address those concerns and come back to us
     with the positive outcomes?
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DR. EISNER: Thanks for the question. 1 has been stated, we've conducted the largest 2 pivotal trial program in CKD anemia, and we have an 3 abundance of data to adequately address the safety 4 and efficacy issues that should enable, we believe, 5 an approval of the product, with appropriate 6 labeling that delineates the safety and efficacy 7 and how the product should be used so clinicians 8 and patients can make those decisions about it. 9 10 As Dr. Little mentioned, we are proposing a postmarketing, real-world data study to test our 11 mitigation strategy of lowering the starting dose 12 and lowering the hemoglobin target. Because 13 roxadustat is a titratable drug and hemoglobin can 14 be measured very readily, we think this strategy 15 will be highly successful, and we are fully 16 committed to further confirming that in a 17 18 postmarketing setting. 19 MS. ALIKHAANI: Thank you. DR. LEWIS: Dr. O'Connor? 20 21 (No response.) Dr. O'Connor, your hand is up. 22 DR. LEWIS:

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Are you muted?
1
              (No response.)
2
              DR. LEWIS: Okay. You are muted, for sure
3
     now.
4
              I'm going to go on for time sake, and I'll
5
      come back to Dr. O'Connor.
6
7
             Mr. Conway?
             MR. CONWAY: Thank you very much. We heard
8
     the FDA talk about, on one of their slides, that
9
10
      overcorrection and overshooting was an issue, and
     we've seen the sponsor's slide deck here on
11
      information that shows it met the first 7 days,
12
     where there is a safety concern, in my opinion, as
13
14
      a patient who's gone through all the different
      things that were described in terms of the burden
15
     of anemia.
16
              I'm trying to figure this out because what
17
18
      it seems to me is that you're trying to give us
19
     assurance on the safety based on modeling, and then
     you're looking at a postmarket study involving
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21
     patients and that type of thing. But in plain
      language, here's my question.
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In plain language, can you tell the patient 1 community that's listening why you should move 2 forward on this if you're relying on a model to 3 show safety and efficacy by reducing dosing and 4 mitigation measures as opposed to waiting and 5 seeing what that actually looks like if you do some 6 other type of study on that? 7 Why should this move forward into a patient 8 population relying on modeling? That I think is a 9 That's my question. Thanks. 10 fair question. DR. EISNER: No. Thanks for the question, 11 and I'll ask Dr. Little to respond to it. 12 DR. LITTLE: Dustin Little here. 13 14 Mr. Conway, there were a few parts to your question. One part had to do with the reliance on 15 I'd like to quickly show you a slide modeling. 16 that does demonstrate from a phase 2 study the 17 18 concept that, indeed, we can see we will have lower 19 rates of hemoglobin rise and fewer overshoots with lower starting doses of roxadustat. 20 21 100 milligrams 3 times a week was the highest starting dose used in the phase 3 studies 22

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for patients who were not on ESA at baseline, and then our recommended starting doses are 50 or 40 milligrams 3 times a week. So in addition to modeling data, we do have clinical data that supports that we will see the expected changes in hemoglobin with lowering the starting dose.

Then the other question that you asked had to do with what we can say to patients. We heard from Dr. Pecoits and from some of the presenters during the open public forum that there is a substantial unmet medical need now for a drug like roxadustat that has an oral mechanism of action that's effective across broad subgroups of patients, including patients for whom ESAs are not particularly effective.

We consider that our data supports a positive risk-benefit ratio currently. We did note some safety imbalances, especially thrombosis and vascular access thrombosis, which we've spoken about quite a bit today. We consider that we can mitigate those risks. We plan to study that. But of course we do consider that those data should be

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in the label, and there should be warnings about that in the label so that physicians can have the option and make considerations regarding the patients in front of them in their office.

Ouestions to the Committee and Discussion

DR. LEWIS: Thank you very much.

I apologize to my other panel members, but we do have six questions, so I think we have to move on. We did get in the unanswered questions from previously and a few other ones, so I apologize. If you'll please put your hands down, we will proceed with the questions to the committee and panel discussions.

I would like to remind public observers that while this meeting is open for public observation, public attendees may not participate, except at the specific request of the panel. After I read each question, we will pause for any questions or comments concerning its wording, then we will open the question to discussion. We will start with question number 1.

Discuss the benefits and risks of roxadustat

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in the non-dialysis-dependent population. 1 Are there any issues or questions about the 2 wording of the question from the panel members? 3 (No response.) 4 DR. LEWIS: I don't see any hands, so if 5 there are no questions or comments concerning the 6 7 wording of the question, we will now open the question to discussion. 8 9 (No response.) DR. LEWIS: The question is open to 10 discussion. I quess I'll start since everyone's 11 12 getting ready to get ready for it. I do think that patients have spoken 13 eloquently of the convenience of not going in to 14 receive an EPO injection, and that's clearly a 15 benefit. That's a convenience benefit. It's also 16 a risk because it means patients could conceivably 17 18 have any physician write them a year's supply of 19 roxadustat and never get another hemoglobin. They do need to go in once or twice a month 20 21 for hemoglobins, and in many places that could be done stat, their injection or subcutaneous 22

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injection given, so I think it has a benefit in a 1 risk. 2 Otherwise, I'm very concerned about the 3 safety signals that we see that are certainly not 4 inferior to those with ESA. I think ESA, if we had 5 known all those safety signals, may have been 6 handled differently when it came before the 7 committee. 8 I do think that those are some of the risks 9 10 that are very serious, and they could be magnified when it's not under study conditions, not having 11 pill counts, not having people reminded three times 12 to come get their hemoglobin, and you might see far 13 more risks or adverse events associated with the 14 risks that have already been described. 15 I'll pause there. I think my first number 16 one is Dr. O'Connor. 17 18 DR. O'CONNOR: Thanks, Julia. 19 Obviously, I have concerns about efficacy on what we've seen, obviously, with hemoglobin going 20 21 up; no issue there. But I'm confused by the quality-of-life data, Julia, and just maybe as a 22

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nephrologist, you and your team could tell me. 1 We've seen significant quality-of-life 2 improvements with iron therapy, for example, in 3 heart-failure patients. Why is it that in such a 4 large study, you can't detect signals of 5 quality-of-life improvement, even with this 6 significant augmentation in improving anemia? 7 The other thing I would say is the 8 9 mitigation program, my guess, with a lower target, 10 would it result in a slightly higher transfusion rate in the active drug and sort of wash out the 11 12 difference between active therapy in the DD patients? 13 14 DR. LEWIS: I guess that was a question to the nephrologists on the panel to some extent. 15 would say that it is surprising that there isn't a 16 quality-of-life signal, and one must wonder if 17 18 there's something offsetting what you would expect 19 to see. You also made another point, which is 20 21 although reduction in IV iron was suggested as a potential benefit, you're right that the cardiology 22

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literature currently has some evidence that it is
1
     actually a benefit to be iron replete, so that's of
2
      interest as well.
3
             Did you want to make any more comments,
4
     Dr. O'Connor?
5
             DR. O'CONNOR: No, that's good.
6
             DR. LEWIS: Do any other nephrologists want
7
      to?
8
9
              (No response.)
             DR. LEWIS: Okay, then we'll go on to
10
      Dr. Bairey Merz, please.
11
12
             DR. BAIREY MERZ: Thank you, Dr. Lewis.
             Noel Bairey Merz. I wanted to mirror
13
14
      Dr. Lewis' summary. I completely agree with her,
     and I would like to also point out and feel
15
      strongly about our citizens' testimonies and how
16
      important it is to them, and yet several pointed
17
18
      out that this would be less costly or even more
19
     cost-effective, and we were not presented with any
      cost data. We're hearing how complicated this care
20
21
      is, and I think we would need to be careful about
     making decisions about cost without any cost data.
22
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I'll also emphasize, if I may, DR. LEWIS: 1 that it is complex. And I, to some extent, 2 disagree with Dr. Fishbane's comments that the main 3 reason that CKD patients are anemic is the 4 logistics of going in for an injection. It is one 5 more trip in some cases, but they have to go in to 6 get their hemoglobin checked. 7 I think the bigger factor is that the 8 complex algorithms to safely deliver this drug are 9 quite daunting, and I think many consider that to 10 be a barrier and are also concerned about the 11 risk-benefit of raising the hemoglobin in the 12 population. So I don't think it's just a logistics 13 14 issue. Our next question is Dr. Packer, or our next 15 discussion. 16 Dr. Packer? 17 18 DR. PACKER: Yes. In my previous comments, 19 I focused on the DD population with respect to all-cause mortality, but I do want to point out 20 21 figure 9 in the FDA document, which shows the effects on all-cause mortality in the NDD 22

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population, which is what we're talking about in
1
      this question.
2
             In all studies, in the OT-plus-7 analysis,
3
4
      they're reporting a hazard ratio of 1.4, a
     confidence interval of 1.08 to 1.82. That's
5
     primarily driven by the 001 study, which was the
6
     biggest of all and had the most deaths. That had a
7
     hazard ratio of 1.68 and a confidence interval of
8
      1.25 to 2.6. These are comparisons with placebo
     with a window of on treatment plus 7 days.
10
             DR. LEWIS:
                          Thank you, Dr. Packer.
11
             Dr. Thadhani?
12
             DR. THADHANI:
                            Thank you, Dr. Lewis.
13
             To add to what you had mentioned, Dr. Lewis,
14
     with regards to the monitoring of individuals in
15
      the outpatient setting, is it fair to say that the
16
      likelihood of overshoot was more common in the
17
18
      outpatient -- or, I'm sorry, in the NDD population
19
      as opposed to the DD population?
             At least from the FDA analysis, that
20
21
      appeared to be the case, which would be consistent
     with your comments about while outpatient at-home
22
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medications may be a convenience, the likelihood of
1
     monitoring or paying more close attention to
2
     monitoring would be more difficult.
3
             DR. LEWIS: Does somebody from the FDA want
4
     to comment on Dr. Thadhani's comment?
5
             Dr. Song?
6
7
             DR. AYACHE:
                          This is Dr. Ayache.
             DR. LEWIS:
                          Oh. Dr. Ayache?
8
                                 In regard to the
9
             DR. AYACHE: Yes.
      overshoot, we saw it in all of the studies in the
10
     NDD population because that's what's compared to
11
12
               As you understand, the initial correction
     phase, there's overshoot as I show in my slide 16.
13
14
             In the DD population, we saw overshooting
     actually in Study 613 and also in Study 64, which
15
     was conducted in the U.S., where the response to
16
     hemoglobin increase was higher in roxadustat than
17
18
      epoetin alfa. Thank you.
19
             Does that answer your question?
             DR. LEWIS:
                          Thanks.
20
21
             DR. THADHANI: Yes, thanks you. That was
     very helpful.
22
                     Thanks.
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DR. LEWIS:
                          Thank you.
                                      And I will remind
1
     everyone, including myself, to state my name before
2
      I speak.
3
              Dr. Wang, you have a question?
4
              (No response.)
5
              DR. LEWIS: Dr. Wang, you may still be
6
     muted.
7
             DR. WANG: Thank you.
                                     Tommy Wang.
8
9
              I just wanted to make a comment, and it
     could be a question --
10
              DR. LEWIS: It's a comment.
11
              DR. WANG: Okay. It's a comment.
12
              I just want to call out the fact, as has
13
14
     been noted a number of times, that for the NDD
     population, in particular, the interpretation of
15
      the MACE and mortality data are really influenced
16
     by whether you're looking at the on-study analysis,
17
18
     which was stated to be the primary analysis, or the
19
     OT-plus-7 analysis.
              I guess the comment is that I do believe
20
21
      that differential dropout most certainly does
      contribute to some of the OT-plus-7 findings.
22
                                                       Ι
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found it fairly persuasive that people who dropped
1
     out of these studies were sicker than the ones who
2
3
      stayed in.
             The issue is whether that's enough to
4
     account for the difference. I guess the thought
5
      experiment is that there was differential dropout,
6
7
     but it was a certain proportion of the patients.
      It wasn't like there are three times as many
8
9
     patients that dropped out. You'd have to have a
10
     pretty large increase in risk in those who dropped
      out compared to those who stay in, I would guess on
11
      the order of 50 to 100 percent increase in the risk
12
      of MACE and all-cause mortality, to fully account
13
      for the difference between the OT-plus-7 and the
14
      on-study.
15
              I guess, again, the comment is I'm not sure,
16
      although there are differences, that we can ascribe
17
18
      that large of a differential. Thank you.
19
             DR. LEWIS:
                          Thank you, Dr. Wang.
             Dr. Soergel?
20
21
             DR. SOERGEL: Thanks, Dr. Lewis.
             David Soergel. I was actually going to make
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a similar comment to Dr. Wang's. I think it's
1
      important to remember that in the
2
     non-dialysis-dependent population, the sponsor
3
      compared to placebo, so we did see this non-random
4
     dropout from the trials and we ended up getting
5
      sicker patients followed through the end of the
6
      study, so therefore, the safety profile might
7
      reflect those differences.
8
             The second thing that I found really
9
10
      interesting is we thought about these two
     populations as being two separate populations, but
11
     when you think of an individual patient
12
      transitioning from late-stage CKD into dialysis, I
13
14
      found the incident dialysis data very compelling,
     where hemoglobin was able to be more adequately
15
     controlled in those patients as the disease
16
17
     progressed.
                   Thank you.
18
             DR. LEWIS: Dr. Cho?
19
             DR. CHO:
                       Hi. My comment is that it's clear
      that roxadustat raises hemoglobin, but I'm not
20
21
      convinced that by decreasing the rise of the
     hemoglobin that we would mitigate the risk of
22
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thrombosis, or infection, or other side effects. 1 Ι think there are mechanisms related to the HIF 2 inhibition that may be predisposing the increase in 3 thrombosis. So I remain quite concerned about the 4 risk mitigation not being able to lower the 5 thrombosis rate. 6 7 DR. LEWIS: Thank you, Dr. Cho. I believe Dr. Cook. 8 DR. COOK: Yes. This is Tom Cook, and I 9 can't directly address this question but I can 10 address the methodology that I've seen today. 11 Actually, I find it strange that I even have 12 to make this comment, but clinical trials are 13 14 fundamentally about assessing causality, and we almost never -- well, I do, but most people in our 15 community don't ever talk about things in terms of 16 causal language. 17 18 We know that -- I hope we know --19 correlation does not imply causation, which means that if we want to assess causality, we need to 20 21 have some formal basis on which we make those decisions. Randomization plus ITT, we know 22

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guarantees that the associations that we see are either random or they're causal because we have removed confounding.

Now, the analyses that we've seen today, most of them, which are based upon these ascertainment windows are not based on ITT, therefore there's no causal basis for doing those analyses, and in my opinion, those analyses are hopefully confounded, and I will ignore them.

So the only analysis that I pay attention to are those which are based upon the full study period, and I would hope that my fellow panel members will seriously discount any of those based on the ascertainment window, especially the 7-day window.

In fact, I would argue I've looked at this question before, and Dave DeMets and I wrote an article in 2019 in JAMA, which we explicitly addressed some of these concerns. And in the data that I've looked at, it's very easy to have a 50 percent or more difference in apparent risk when one does this kind of arbitrary censoring based

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upon time on treatment.
1
             I mean, in fact, it's the tail wagging the
2
      dog because the reason that people don't continue
3
4
      treatment is usually related to their clinical
      status, and if their health is failing and they
5
     become at high risk for mortality, then they're
6
     likely to discontinue treatment. And therefore,
7
      these kinds of analyses are just fundamentally
8
9
     broken, and I will pay no attention to them.
10
      you.
             DR. LEWIS: But the analyses that showed
11
      safety signals that were the ITT analysis, you
12
     would put weight or at least --
13
14
             DR. COOK: I would, yes.
             DR. LEWIS: -- consider.
15
             DR. COOK: Yes, I would.
16
             DR. LEWIS:
                          Thank you, Dr. Cook.
17
18
             I believe Dr. Packer is next.
19
             DR. PACKER:
                           I just wanted to ask Dr. Cook a
                 The concept of intention to treat in any
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21
      trial is that you start out with some assurance of
     balanced populations at the start of the study
22
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because of randomization, and then you follow all 1 patients for the planned duration of therapy and 2 count all events, whether people stay on treatment 3 or not. 4 When you do that, that's a true ITT 5 analysis, and what we're seeing today doesn't 6 approximate that standard, either the on-treatment, 7 the on-treatment plus 7 days, or the on-treatment 8 9 plus 28 days. None of those approximate a true ITT 10 analysis. So if you wanted to really adhere to ITT, 11 you would discount everything we've looked at today 12 in the NDD population. Now, the DD population is a 13 little bit different because the retention rates in 14 the two groups are actually similar or even favor 15 epo. 16 Dr. Cook, do you really think that 17 18 on-treatment here represents an intention-to-treat 19 population? I don't think so. No, I agree a hundred percent. 20 DR. COOK: 21 This is Tom Cook. I agree a hundred percent. DR. PACKER: Yes. 22

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DR. COOK: What Dave DeMets and I say in our 2019 JAMA paper is if you see a difference or the lack of difference between two arms, it's due to one of three things, either chance, causation, or confounding. And what randomization does, is it eliminates the confounding. So now you look at your confidence intervals and your p-values, and you say this likely could be due to chance. And if you rule out chance, then you know it's causal. If I condition on being on treatment plus some period of time, I actually reintroduce confounding for the very reasons that have been discussed, except they haven't been framed in terms of causal language. In fact, I would argue that even in the DD population --DR. LEWIS: If I may, I think we're straying from the question --DR. COOK: Yes. But the question is how do you evaluate the evidence that's in front of us? Yes. Thank you. DR. LEWIS: We have six questions and 30 minutes, so I think I'm going to move on to the second question,

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and perhaps some of you, Dr. Wang, can put your 1 comments into the second question. 2 I'm now going to read the second question. 3 If you have concerns regarding these risks, 4 discuss whether you believe they could be addressed 5 through modification of the treatment algorithm, 6 for example, changes in target hemoglobin, starting 7 dose, titration scheme, and monitoring paradigm. 8 If you favor changes to the treatment 9 algorithm to enhance safety, discuss whether they 10 should be tested prior to approval, after approval, 11 12 or not at all. Are there any questions about the wording of 13 14 the question? Dr. Cook, do you have your hand up for a 15 question about the wording of the question 16 number 2? 17 18 DR. COOK: No, I just forgot to put it down. 19 Thank you. DR. LEWIS: 20 Okay. 21 So if there are no questions or comments concerning the wording of the question, we will now 22

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open the question to discussion.
1
             Dr. Crowley?
2
3
              (No response.)
             DR. LEWIS: Dr. Crowley, you're on mute.
4
             DR. CROWLEY: Yes.
                                  Thank you.
5
             I think this concept is really a very
6
7
      desirable patient-centered approach to treatment of
      anemia, and I think we can all agree that there's
8
9
      demonstrated efficacy. But it seems like the real
      challenge here is can we control the risks that are
10
      associated with any ESA, including roxadustat in
11
      this particular consideration.
12
             In terms of these modifications of the
13
14
      treatment algorithm, I guess the question is, can
      the prescription of this drug come with sufficient
15
      instructions and confidence that these would be
16
      followed, excluding certain patients who would be
17
18
      at extremely high risk for prothrombotic agents,
19
      for ensuring that providers know what they're doing
     with this medication and have a system in place to
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21
     monitor? It's not enough just to prescribe it, but
      you have to have a recommended monitoring process.
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Can we have sufficient public education such 1 that people appreciate that it's not that you're 2 just going to get a pill and you don't need 3 monitoring; you're still going to need monitoring. 4 That really is a concern, that people think I can 5 just take the pill and I don't have to get my 6 hemoglobin checked. 7 So I think those are the concerns that I 8 would have with regard to how can we mitigate these 9 I think it's possible, but that's really 10 where I worry most, I think. 11 12 DR. LEWIS: Thank you, Dr. Crowley. Dr. Packer? 13 14 DR. PACKER: Yes. I think what the sponsor is proposing seems like a very reasonable approach 15 that needs to be tested. What we don't know is the 16 degree to which the risks that we see, whether it 17 18 be thrombosis, all-cause mortality, infection, 19 whether these risks are related to the rapid increase in hemoglobin or whether it's due to 20 21 potentiation of hypoxia-inducible factor 1 alfa. That uncertainty is not going to be resolved by a 22

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stimulation; that uncertainty needs to be resolved 1 by an actual trial. 2 I agree completely, and I think 3 DR. LEWIS: the trial needs to be prior to approval, and the 4 hypothesis that the dose adjustments and different 5 algorithms will mitigate those safety signals needs 6 to be tested. 7 Further, I would actually think there's 8 enough of a safety signal that there may need to be 9 a formal dedicated cardiovascular study not like 10 what was demanded of the hypoglycemic drugs. 11 also have a concern about their ability to be able 12 to do the postmarketing study because of not being 13 able to find enough patients left on ESA to match. 14 So all those things concern me in answer to 15 those questions. 16 Dr. Parsa? 17 18 DR. PARSA: I was about to lower, but I 19 guess I'll reiterate it because what I was thinking was also said by others. Sorry. This is Afshin 20 21 Parsa. I think that, yes, as mentioned before, the 22

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ability to understand the risk here is we simply 1 don't have sufficient data to make anything that's 2 definitive enough. The suggestions that were made 3 in terms of changing the hemoglobin target, 4 starting dose, all sound reasonable, but I think 5 those need to be really assessed prior to approval. 6 I have concerns about trying to do this in a 7 postmarketing setting once it's set free out there 8 9 without being properly controlled. I don't think we're going to get the necessary information 10 without doing the proper trial first. 11 DR. LEWIS: Thank you, Dr. Parsa. 12 Mr. Conway? 13 14 MR. CONWAY: Thank you very much. wanted to say I think Dr. Crowley characterized 15 perfectly, at least from my standpoint as an 16 [inaudible - audio gap] -- leader. 17 18 The frustrating thing here is the patient 19 burden that's been articulated, especially during the public comment, I believe is a hundred percent 20 21 accurate. And I have to tell you, having lived with anemia, trying to get a transplant, trying to 22

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keep a full-time job -- at the time I was the 1 deputy secretary for the State of Virginia -- just 2 to make it [indiscernible - audio feedback] --3 Friday, come Monday, my epo started tapering down. 4 It's a tremendous burden, and what we're 5 looking at is a vehicle through which patients 6 could theoretically have less burden, which is 7 [inaudible]. So that's kind of the idea. However, 8 when we get down to the drug itself that we're 9 talking about, I'm very concerned about this idea 10 of taking the data that we have and try and 11 12 extrapolate from that, through a model or through some other kind of tangential effort, in my 13 14 opinion, to show that there is safety. So the frustrating thing in listening to 15 this, for me, is that the patient burden is well 16 documented, in my opinion, but the burden is on the 17 18 sponsor to show why this should move forward before 19 it's tested out as opposed to waiting and doing that postmarket. I think we should get it checked 20 21 out before it goes into patients. I really do. Thank you. 22

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I also will make a comment that DR. LEWIS: 1 once we know what the appropriate dosing is and 2 perhaps the other study has done it, another 3 consideration is a REMS program, where only 4 physicians who have gone through a certain amount 5 of education are allowed to prescribe it. You do 6 one month's supply, and if the patient doesn't show 7 up for their hemoglobin, to make sure that the dose 8 is still correct for them. 9 They run out. That's another consideration that the FDA 10 could consider to mitigate some of the concerns 11 12 that have been expressed by the committee. Are there any other comments? 13 14 Mr. Conway, your hand is still up, and I wasn't sure if it was still up or you had another 15 comment. 16 MR. O'CONNOR: No, I don't. Thank you very 17 18 much. I'll take it down. Okay. 19 DR. LEWIS: I'm going to make an attempt to summarize the comments on question 1 and 20 21 question 2, and just for time sake, I decided to put them together. 22

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I think the multiple members of the committee have expressed the benefit of less travel to get injections, especially for patients who live far away, and I also really appreciate the patients who made that clear to us during our open session, so we understand that part of it.

Expressed concerns about the safety of the drug itself, such as the concerns about mortality expressed by Dr. Packer, the concerns about overshoot expressed by Dr. Thadhani, and the concerns about even if you look at comparing the OT-7 to the on-study, that there would have to be a tremendous increased risk to explain the mortality in the people who dropped out. Another benefit I forgot to mention that Dr. Soergel mentioned was the very big benefit of an instant hemoglobin is better in people transitioning from CKD and non-dialysis to dialysis.

There is also obviously a concern about other adverse events that are not related perhaps to the hemoglobin or to the proposed mitigation

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strategy because of other effects of HIF inhibitors 1 that could contribute to infections and other 2 3 things. We appreciate Dr. Cook's statistical input 4 on the analysis that are most informative to look 5 at. I think there were several people that were 6 concerned about doing the study after 7 postmarketing, and that maybe prior to approval, 8 finding the right dose and seeing if it mitigates 9 10 some of the adverse events might be important. lastly, I mentioned considering a REMS program. 11 If there is no further discussion -- and 12 I'll pause in case someone wants to raise their 13 hand or feels I missed something in that 14 summary -- we will move on to question 3, which is 15 a voting question, and Dr. Joyce Yu will provide 16 the instructions for the voting. 17 18 DR. YU: Thank you. 19 Hi. This is Joyce Yu. Question 3 is a voting question and voting members will use the 20 21 Adobe Connect platform to submit their votes for this meeting. After the chairperson has read the 22

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voting question into the record and all questions and discussion regarding the wording of the vote question are complete, the chairperson will announce that the voting will begin.

If you are a voting member, you will be moved to a breakout room. A new display will appear where you can submit your vote. There will be no discussion in the breakout room. You should select the radio button that is the round circular button in the window that corresponds to your vote, yes, no, or abstain. You should not leave the "no vote" choice selected.

Please note that you do not need to submit or send your vote. Again, you need only to select the radio button that corresponds to your vote. You will have the opportunity to change your vote until the vote is announced as closed. Once all voting members have selected their vote, I will announce that the vote is closed.

Next, the vote results will be displayed on the screen. I will read the vote results from the screen into the record. Next, the chairperson will

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go down the roster and each voting member will
1
     state their name and their vote into the record.
2
      You can also state the reason why you voted as you
3
     did, if you want to. However, you should also
4
     address any subparts of the voting question, if
5
      any.
6
7
             Are there any questions about the voting
     process before we begin?
8
9
              (No response.)
              DR. LEWIS:
                          Thank you, Dr. Yu.
10
              If there are no questions, I will read the
11
     voting question.
12
              Should roxadustat be approved for the
13
      treatment of anemia due to chronic kidney disease
14
      in adult patients not on dialysis? If not, provide
15
      your rationale, as well as recommendations for
16
     additional data and/or analyses that would support
17
18
      a favorable benefit-risk profile and approval of
19
     roxadustat.
             Are there any questions about the wording of
20
21
      the question?
              (No response.)
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DR. LEWIS: If there are no questions or
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      comments concerning the wording of the question, we
2
     will now begin the voting on question 3.
3
              (Voting.)
4
             DR. YU: The voting has closed and is now
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      complete. Once the vote results display, I will
6
      read the results into the record.
7
              (Pause.)
8
9
             DR. YU:
                      Thank you.
             The vote results are now displayed.
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                                                    I will
      read the vote totals into the record.
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      chairperson will go down the list and each voting
     member will state their name and their vote into
13
      the record. You can also state the reason why you
14
     voted as you did, if you want to. However, you
15
      should also address any subparts of the voting
16
      question, if any.
17
18
             The vote total is 1 yes, 13 noes, and zero
     abstentions. Thank you.
19
             DR. LEWIS:
                          Thank you.
20
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             We will now go down the list and have
      everyone who voted state their name and vote into
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the record. You may also provide justification for
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      your vote if you wish to. However, please remember
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      to address any of the subparts of the question that
3
      correspond to your vote.
4
             We'll start with Dr. O'Connor.
5
             DR. O'CONNOR: Christopher O'Connor.
6
      answered no. I'm concerned about the totality of
7
      information with respect to adverse safety signals,
8
     and I don't believe we understand whether the
9
     mitigation strategy dose will be safe. Thank you.
10
             DR. LEWIS:
                          Thank you.
11
             Dr. Crowley?
12
             DR. CROWLEY: Susan Crowley. I voted yes.
13
      I think that with the significant patient burden of
14
     anemia, the associated risks with any ESA that are
15
      similar in roxadustat, a fair way potentially to do
16
      this is to allow patients and providers to do
17
18
      shared decision making under a REMS program to try
19
      to mitigate some of the risks that may be increased
     with roxadustat.
20
21
             I thought that was a potential opportunity
      to allow for the use of this medication to meet an
22
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294
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unmet need, to address patient suffering, and to
1
      try to control risks.
2
3
             DR. LEWIS:
                          Thank you.
             Dr. Cook?
4
             DR. COOK: Yes. Thomas Cook. I voted no,
5
      and this was difficult for me. But ultimately I
6
     had to listen to the people who thought that the
7
      safety profile wasn't established, especially for
8
9
      the proposed new dosing strategy that the sponsor
      is discussing. I didn't think that their
10
      observational study that they proposed would
11
     actually answer the questions of interest.
12
13
     you.
14
              DR. LEWIS:
                          Thank you, Dr. Cook.
             Dr. Kasper?
15
                          Dr. Ed Kasper. I voted no.
              DR. KASPER:
                                                          Ι
16
     would like to see the mitigation strategy tested
17
18
     prior to a revote or representation of this
19
     particular drug.
                          Thank you, Dr. Kasper.
20
             DR. LEWIS:
21
              Dr. Packer?
22
              (No response.)
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DR. LEWIS: Dr. Packer?
1
             DR. PACKER:
                           Sorry. I was needed.
2
             Milton Packer. I voted no. I share the
3
      reason that Dr. O'Connor, Dr. Cook, Dr. Kasper have
4
     already expressed.
5
             I noticed that the sponsor has done all the
6
7
     clinical trials using a very specific strategy, but
     now would like approval for a strategy which has
8
     been developed only as a simulation. If they
9
     really want people to use the new strategy in
10
     clinical practice, they really do need to test it
11
     and show its efficacy and safety.
12
             DR. LEWIS:
                         Thank you, Dr. Packer.
13
14
             Dr. Wang?
             DR. WANG: Yes. Thomas Wang. I voted no,
15
      again, for the reasons stated by my colleagues.
16
      did find the safety data not clear-cut for the
17
18
      reasons mentioned, but the totality of the safety
19
     data somewhat unsettling. I was concerned that
     more definitive data to address this question would
20
21
     have been difficult to obtain in the postmarketing
22
      setting, so that's the reason for my vote.
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22

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296 DR. LEWIS: Thank you. 1 Dr. Thadhani? 2 DR. THADHANI: Thank you. Ravi Thadhani. 3 voted no for the reasons stated. I found the 4 analysis, with the biased included, difficult to 5 interpret. 6 The only comment, without being redundant, I 7 would make is in looking at how to move forward, I 8 think we just need to acknowledge that this 9 data set of non-dialysis patients is and will be 10 the largest data set we have with regards to 11 efficacy and safety, and before jumping into yet 12 another clinical trial, to look carefully as to 13 what clearly we would need in the most efficient 14 fashion to get this to the finish line if that's 15 the direction that others and the agency feel is 16 possible. Thank you. 17 18 DR. LEWIS: Thank you, Dr. Thadhani. 19 Dr. Conway? MR. CONWAY: Paul Conway. I voted no, with 20 21 difficulty. As much as I am a champion of patient

care, choice, and innovation, I did not feel as

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though the safety information presented was
1
      adequate. And I would like to see the mitigation
2
      strategy tested before we roll out to patients that
3
     are very vulnerable in the middle of COVID-19, but
4
     also patients that depend upon vascular access and
5
      other things to keep life going. I think there's
6
     higher burden to show for safety.
7
                          Thank you very much, Mr. Conway.
             DR. LEWIS:
8
             Dr. Cho?
9
             DR. CHO: Hi. Leslie Cho. I voted no for
10
      the reasons that everyone has stated. I do not
11
      think the rise in hemoglobin is the cause of all
12
      thrombosis and all side effects. It's uncertain to
13
     me whether that really is the cause and whether it
14
     really is HIF inhibition that may be the cause of
15
      the thrombosis. Until we test the lower dose in
16
     patient population, I find it not a viable
17
18
      solution.
19
             DR. LEWIS:
                          Thank you, Dr. Cho.
             Dr. Merz?
20
21
             DR. BAIREY MERZ: Hi. Noel Bairey Merz.
                                                         Ι
                 I thought it was quite a clear safety
22
     voted no.
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signal and an unclear convenience or access signal. 1 I also thought that FDA approval on modeling 2 mitigation strategies would be stepping out of the 3 bounds of certainly what we traditionally do. 4 Thank you, Dr. Merz. 5 DR. LEWIS: Ms. Alikhaani? 6 7 MS. ALIKHAANI: Yes. Jacqueline Alikhaani I voted no. It was a very tough decision here. 8 9 for me because I really value the patient voice, the consumer voice, and the testimony of the 10 patients was very strong and clear that there's a 11 need to get improved care for them, and improving 12 care means safety first, to me. 13 I have family members living with this 14 dreadful disease and it matters a lot on many 15 levels for me, so it's not an easy decision to say 16 I think we do need major risk mitigation and 17 18 accountability assurances to be in place to create 19 the right pathway for approval for roxadustat. I hope we can do that in the future. And whatever 20 21 is done, I hope that we can also have a team of patients, and caregivers, and family members as 22

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part of the leadership team for the trial, and the
1
      research to make sure their voices are there and
2
      they're completely informed about all of the
3
     different issues at stake, especially safety.
4
             DR. LEWIS:
                          Thank you.
5
             I voted no, and I agree with all my
6
     colleagues' previous comments.
7
             Dr. Moliterno?
8
9
             DR. MOLITERNO: Oh, you're good, Dr. Lewis.
                  David Moliterno. I voted no.
             Hi.
10
      rewrote the question, which I won't, I think I may
11
     have answered it differently. I do think the drug
12
     has merit, but the question posed was the data
13
14
     given to us as presented by the applicant.
             I think, in short, I agree with
15
     Dr. Thadhani. I think there's a rich data set here
16
      that needs to be dwelled on further and dug into.
17
18
     You remember my comment at the very beginning to
19
      the agency, and Dr. Unger's response that they just
      received this risk mitigation strategy and those
20
21
      related data recently. So I think it will take
     more digging, and more time, and more thinking.
22
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Maybe this group will have the opportunity to 1 reconsider this compound at a future time. 2 DR. LEWIS: 3 Thank you. Dr. Parsa? 4 This is Afshin Parsa, and I 5 DR. PARSA: voted no. Having treated many patients, I 6 certainly empathize with the logistic challenges 7 and the patient burden. I really wanted this to be 8 available as a choice for treatment, but I'm simply 9 too concerned about the safety signal and think 10 that we still need to work out more of these 11 12 details before this can go forward. DR. LEWIS: Thank you very much. 13 14 I'm going to summarize quickly. I think that the consensus is that the safety signal is 15 concerning to the panel members, concerning enough 16 that they feel that a mitigation study needs to be 17 18 done prior to approval. I think that many people, 19 including Dr. Crowley who voted yes, but many other people -- and I really appreciate our consumer and 20 21 patient reps here -- are very empathetic to the patient's voice of wanting an oral or an easier 22

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1 therapy, but not at the expense of unknown or perhaps negative safety profile. 2 I think it's also important to note that 3 4 there is concern about effects that will not in any way be related to the hemoglobin rise or to the 5 mitigation study that's being proposed to be done 6 at the recommendation of this committee prior to 7 approval. 8 I think the points were well made that there 9 should be a very careful consideration for what 10 will most efficiently and effectively answer this 11 question in a study, and I applaud us being 12 reminded that we should include patients' and 13 families' voices in feedback on that design as 14 well. 15 We will take a short five-minute break now. 16 Panel members, please remember that there should be 17 18 no chatting or discussion of the meeting topic with 19 anyone during the break . We will resume at 4:35 Eastern Standard Time. 20 21 (Whereupon, at 4:30 p.m., a recess was taken.) 22

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DR. LEWIS:
                          Okay. We will now go on to
1
      question 4.
2
              Discuss the benefits and risks of roxadustat
3
      in the dialysis-dependent population.
4
             Are there any issues or questions about the
5
     wording of this question?
6
7
              (No response.)
              DR. LEWIS: If there are no questions or
8
      comments concerning the wording of the question, we
9
     will now open the question to discussion.
10
             Will the panel members please raise their
11
     hand to participate in the discussion.
12
              Dr. Packer?
13
14
              (No response.)
              DR. LEWIS: Dr. Packer, you're still muted.
15
              DR. PACKER: Julia, I really apologize.
16
     keep forgetting to unmute myself.
17
18
             Here I think the data are a little bit
19
      easier to interpret because the differential
      dropout issue is less marked. In fact, the
20
21
      retention rate was actually greater in the epo
      group than the roxadustat group.
22
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So we don't have a lot of the complications
1
     of the data that we had in the NDD population, and
2
3
     here we have a comparison with a drug which is
     already labeled for increase in mortality and
4
     increase in risks and we're seeing estimates here
5
     that are either similar to or greater than those
6
7
     seen with epo.
             I quess I'm really concerned about
8
9
     Study 613. 613, as the a sponsor said, had a
     little bit higher dose of roxadustat and maybe a
10
     little bit lower dose of epo, and the mortality
11
     differences became even more marked. So there's
12
     something that this drug is doing that is maybe
13
14
      different than epo. And we already know about
     epo's risks, and they're in the label, so this is a
15
     source of concern.
16
             DR. LEWIS:
                         Thank you, Dr. Packer.
17
18
             Dr. Crowley
19
             DR. CROWLEY: Yes. Thanks.
             As Dr. Packer was saying, I think we can
20
21
     have a little greater confidence in the study
      results because we don't have that attrition bias,
22
```

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and I think we see, at least for the primary 1 analysis for MACE, fairly neutral results. 2 I think in addition to that, we can have 3 great confidence in terms of the control, the risk 4 mitigation, because patients are coming three times 5 a week for those that are doing in center, or if 6 they're at home, we know they're on home dialysis, 7 they're connected with a clinician, so their 8 follow-up, I think we can have more confidence that 9 patients will understand what this medication is 10 about and that they require monitoring, and we have 11 12 an opportunity for doing that monitoring. For here, I feel a lot more confident with 13 14 this for the dialysis population, although I see the greatest opportunity for the non-dialysis CKD 15 population. 16 17 DR. LEWIS: Thank you. 18 Dr. Wang? 19 DR. WANG: Yes. Tommy Wang. I just wanted to call out the helpful 20 21 comments of Dr. Cook in the last session about the potential strong effects of differential dropout, 22

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which we talked at length about for the NDD 1 population. Based on his comments, I would say 2 here, as previously pointed out, the attrition 3 rates were much less different and we have an 4 on-study analysis in the DD population shown in 5 figure 12 of the FDA analysis, which show some 6 confidence intervals for MACE and all-cause 7 mortality that exclude one in the unfavorable 8 direction for roxadustat. 9 That finding makes me concerned. And on top 10 of that, as Dr. Packer has noted, the comparison 11 group here is already a drug for which there have 12 been safety signals and a warning attached to it. 13 14 So again, I think in its totality these safety data are not satisfying. Thanks. 15 Thank you, Dr. Wang. DR. LEWIS: 16 Dr. O'Connor? 17 18 DR. O'CONNOR: Chris O'Connor. I just would 19 add to what was said previously, that really applies to the DD populations, that the extremely 20

important RBC transfusion rate advantage is less in

this population. With the mitigation strategy

21

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dose, it's unclear, if you look at CO-46, whether
1
      that would even hold up with the lower dose.
2
      think one of the added benefits of this therapy may
3
     be attenuated.
4
             DR. LEWIS:
5
                          Thank you.
             Dr. Parsa?
6
             DR. PARSA: Afshin Parsa. Yes. Here I'm
7
     also seeing that the risk profile is easier to
8
9
     assess, as others have said, and maybe not as
     worrisome. But then the question becomes, what is
10
      the benefit?
11
             We still have an increase, obviously, and
12
      some trend towards death in Study 613.
13
14
     Kaplan-Meier increases over time, suggesting that
     maybe it's not just rate of change of hemoglobin,
15
     but not enough data to really conclude anything
16
     based on that. But there's still increased
17
18
      thrombosis, access clotting, which we all know as a
19
     nephrologist is a nightmare to deal with, as well
      as the patients, it's worse for them.
20
21
             That's still a question, what's the benefit
     here when we're still seeing a signal for risk?
22
```

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The convenience of the PO and decreasing the 1 patient burden, which is high, is really not 2 modified that much in this circumstance. 3 However, one subgroup that I was thinking in 4 which it might be different here are 9 or 5 10 percent of the dialysis population that are 6 7 resistant to epo treatment, so really high ferritin, or they're just not responding, or you 8 9 can't get them well. 10 In that smaller subgroup, there might be some potential benefit here based on these signals 11 that could mitigate some of those [indiscernible], 12 thrombosis, or other risks that we've seen, but 13 14 certainly not as a whole. But I do want to make the distinction between that subgroup and the rest of 15 the population. 16 DR. LEWIS: Dr. Thadhani? 17 18 DR. THADHANI: Thank you, Dr. Lewis. Thadhani. 19 Just to clarify the transfusion issue, I 20 21 think the comment was made, and that is correct, that the benefit of this treatment is treatment of 22

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anemia and obviously reduction of transfusion.
1
      think an aggregate may not have been seen, but I
2
     believe -- and again I apologize that I may not
3
     have all the details -- in Study 064, there was a
4
      reduction in transfusion, which is the US-only
5
      study, I believe, obviously paying close attention
6
     to that, including over 40 percent of
7
     African Americans in that particular study.
8
             I understand the design was such that rescue
9
      therapies involved ESA and then transfusion for the
10
      roxa arm. But that said, there was, I believe, a
11
      reduction in transfusion in 064 but was not seen in
12
      063 and 002. Thank you.
13
14
             DR. LEWIS: Dr. Packer, I believe your hand
      is up again. I don't mean it negatively.
15
      actually asking you is it up again?
16
             DR. PACKER: No, it's not. I'm sorry.
17
18
             DR. LEWIS: Dr. Crowley, your hand is up.
19
     Okay.
             Dr. Cook?
20
21
             DR. COOK: Yes. I just want to comment that
      it's not my concern about the differential in
22
```

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1
      dropout, it's the rate of dropout. It still breaks
      ITT if the rates are the same but the rationale
2
     underneath is different, the reasons for dropout.
3
4
     So I'm not convinced just because they're the same
     that that actually improves my understanding of the
5
      overall result.
6
7
             DR. LEWIS: Thank you, Dr. Cook.
             Dr. Soergel?
8
9
             DR. SOERGEL: Thanks, Dr. Lewis.
10
             My view is that based on the FDA-agreed
      analysis, which is beyond therapy plus 7 days, the
11
      data look reassuring for MACE and for all-cause
12
     mortality. There's clear efficacy in this
13
14
     population, and there's been little innovation in
      this space in many years. So I think there's a
15
     place for this medicine, as was commented earlier;
16
      so that's my view.
                          Thank you.
17
18
             DR. LEWIS: Dr. Cook your hand is up.
                                                      Do
19
     you have another comment?
                              Sorry. I forgot to put it
20
             DR. COOK:
                        No.
21
      down.
             DR. LEWIS: I wonder if our patient
22
```

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representative or our consumer representative have
1
      a comment.
2
3
              (No response.)
             DR. LEWIS: While they're thinking,
4
     Dr. Packer?
5
             DR. PACKER: Julia, could I ask a guestion?
6
7
      There appears to be a group of patients who are
      resistant to erythropoietin, and these were
8
     patients with a lot of inflammation. It's a
9
10
                I'm not certain how big the subgroup is,
      subgroup.
     but these are patients for which epo is not a
11
     particularly viable option because they don't
12
      respond to it, and they do respond to this drug.
13
             I'm just wondering whether there is a
14
      subgroup of the dialysis-dependent patients that
15
     would actually have an option here that they don't
16
     have with epo because of epo resistance.
17
18
             DR. LEWIS:
                          Thank you, Dr. Packer.
19
             Mr. Conway?
             MR. CONWAY:
                          Thank you. I'm actually
20
21
     wondering the same thing, and based on the data
      that was presented, it could be an effective tool
22
```

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for part of that population.
1
             Incredibly, for me, as an advocate, I
2
     believe it should be tested out before it's
3
4
      deployed. I'm not satisfied with the safety
      information. It's close, but I'm just not
5
      comfortable of it holding up as a package in terms
6
     of what we're looking at. Thank you.
7
             DR. LEWIS:
                          Thank you.
8
             Ms. Alikhaani? I should ask you for
9
     permission to call you Ms. Jacqueline so I don't
10
      destroy your name every time. I apologize.
11
      really bad at names, but you have your hand up.
12
              (No response.)
13
             DR. LEWIS: Ms. Alikhaani?
14
              (No response.)
15
             DR. LEWIS: You may be offline. Actually, I
16
     don't see her phone. While we're waiting to get
17
18
     her back online, I'll make a quick comment.
19
             I also was impressed with the data that
      showed that the roxadustat group could raise their
20
21
     hemoglobins in the epo-resistant kind of inflamed
      group, but what's surprising is that it doesn't
22
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translate, or it doesn't obviously translate, or
1
     wasn't physically translatable, into any harder
2
                 In fact, there were more infections and
3
     more thrombosis.
4
             I asked specifically if they had seen any
5
     positive things besides a higher hemoglobin --
6
     which is of value, don't get me wrong -- and I
7
     guess they did not or they did not do the analysis.
8
             I think we're back online.
9
             Ms. Alikhaani?
10
             MS. ALIKHAANI: Yes?
11
             DR. LEWIS: Your question or comment?
12
             MS. ALIKHAANI: I think I got kicked out
13
14
      again.
             Can you hear me?
             DR. LEWIS: Yes.
                                Sorry we got you kicked
15
     out; glad we got you back.
16
             MS. ALIKHAANI: Okay.
                                     Thank you.
17
18
             I'm a big champion of diversity in clinical
19
     trials because every patient is an individual and I
      think that matters a lot, and the more diversity
20
21
     you have, the better. I was a little bit dismayed
      that we had such a small amount of African
22
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Americans in the trial who documented as having the greatest disparities in care for heart disease and other related conditions.

So I really think education and awareness is very important, in general, for these conditions -- not this medication -- and the more we engage with the community, and the patients, the caregivers, the family members, and everybody involved in the trial, and the research from start to finish, I think we're going to have better outcomes all around.

I think it's really critical, and that way we can make sure the trials are designed with the patients right up front with everybody else, and also not just on the table but also at the leadership table for the trials. Hopefully that way we can get these kinds of treatments voted in because I really wanted to vote for this; I really did. I was very hopeful. So hopefully we can get something done in the future.

DR. LEWIS: I particularly appreciate that comment. I actually wrote it down as an intended

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comment myself, but for time sake hadn't mentioned
1
      it.
2
              For the non-nephrologists, African Americans
3
     make up about 12 to 15 percent of our population,
4
     but 33 percent of our dialysis population.
5
      tends to also track with social determinants of
6
     health, which are known to affect medication
7
      adherence. I think the underrepresentation,
8
     particularly in the trials overall, of only
9
10
      8 percent, blacks are of concern and unfortunate,
      and hopefully something that could be addressed in
11
      the efficient design of a new trial.
12
              Thank you for bringing that up.
13
14
             MS. ALIKHAANI: Thank you.
             DR. LEWIS: Are there any other comments?
15
              (No response.)
16
              DR. LEWIS: Okay.
                                 If there are no other
17
18
      comments, I will try to summarize our comments to
19
     this question.
              I think that, in general, the committee felt
20
21
      that because there wasn't an uneven follow-up as
     much in this trial, in fact, if anything, a little
22
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bit more ESA retention but still not a big differential, that the data was easier to interpret. However, the on-study data and the 613 study were of particular concern since many of the MACE things excluded one unfavorable direction for roxadustat, so that remains a concern.

Then there was an issue of what potential benefit is if there were not as big a reduction in transfusions. It was also confounded by the ability to receive ESA. Then, of course, for the patients that are on hemodialysis and going to a center, the benefits of less travel, et cetera, would be missing. The potential safety signal of access clotting was particularly noted to be lifelines for our patients now who are fortunately living long enough on dialysis compared to decades ago, that they do run out of the access.

One group of interest to several panel members were those who are resistant to epo and the potential for this drug to particularly help those patients have a higher hemoglobin.

Let me just glance down the way. Also, I

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think the point was made for the first time that 1 it's very important, like we just finished talking 2 about, the underrepresentation of African Americans 3 in the global trials as a whole. Study 064 did 4 have a good representation but had increased 5 deaths, so it still remains a concern. 6 If there's no further discussion on this 7 topic, I will now read question number 5. 8 If you have concerns regarding these risks, 9 discuss whether you believe they could be addressed 10 through modification of the treatment algorithm, 11 for example, changes in target hemoglobin, starting 12 dose, titration scheme, and monitoring paradigm. 13 If you favor changes to the treatment 14 algorithm to enhance safety, discuss whether they 15 should be tested, 1) prior to approval, 2) after 16 approval, or 3) not at all. 17 18 Are there any issues or questions about the 19 wording of the question? (No response.) 20 21 DR. LEWIS: I don't see any hands raised. So if there are no questions or comments concerning 22

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the wording of the question, we will now open the question to discussion. Panel members, please raise your hand and identify yourself.

Dr. Parsa?

DR. PARSA: Afshin Parsa. Just following up on what I've said in response to question 4, which leads into this, it is not so much in terms of the treatment algorithm being different than what was proposed as an update from the applicant, but so much the risk-benefit ratio and then the subgroup of those who are epo resistant.

I do think that since the risk is modest overall, there's still concern. People with epo resistance certainly can be an issue, and I don't mean someone who's epo resistant for a few weeks because of a minor infection, but those that are really more chronically hyporesponsive, requiring high iron and still not being able to get a stable hemoglobin level there.

There is the potential that that group could fall in the category of -- if one defines it properly and has reasonable thresholds, or there is

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[indiscernible] and forgets it, to then have some 1 postmarketing follow-up to see how they do while 2 the rest is working there. But even though it's a 3 smaller number of dialysis patients, it's still not 4 an insignificant number, and it could change the 5 risk-benefit ratio, potentially. 6 Thank you, Dr. Parsa. 7 DR. LEWIS: Do other committee members have comments on 8 9 this question? 10 (No response.) DR. LEWIS: You could be able to comment 11 12 again on whether you think the treatment algorithm to enhance safety should be done prior to approval, 13 14 after approval, or not at all because you might have a differential feeling about it than you would 15 for the non-dialysis population. 16 Dr. Packer? 17 18 DR. PACKER: Yes. Julia, I think you're 19 asking us to express our views so that it makes it easy for you to summarize the sense of the 20 21 committee. I think the principle is that we described 22

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earlier, that the proposed changes in dosing are 1 based on simulations, and we don't know, in the 2 absence of clinical trial evidence, whether those 3 proposed dosing changes will mitigate the risks. 4 Then there's the other issue that it is 5 possible that the proposed dosing changes will not 6 match the efficacy of epo. We already have a 7 situation where in our randomized trials, the 8 retention rate is higher in the epo group than the 9 roxadustat group, and if we lowered the dose of 10 roxadustat, will that retention difference become 11 12 even greater. So essentially, the proposed dosing regimen 13 should be tested in a clinical trial as opposed to 14 being relying on the simulation. 15 Thank you, Dr. Packer. DR. LEWIS: 16 Dr. Crowley, do you want to comment on 17 18 whether you favor any postmarketing study, 19 premarketing study, for the dialysis-dependent population? 20 I guess the sponsor had 21 DR. CROWLEY: Yes. eluded to, or stated actually, that they were 22

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planning to reduce the dose. And perhaps an
1
      assumption I'm making is that they would be in fact
2
     potentially trying to capture that data to inform
3
     us about specifically the question that was just
4
      raised, about whether efficacy is maintained and
5
      risk is reduced.
6
             DR. LEWIS:
7
                          Okay.
             DR. CROWLEY: So I don't know if we can make
8
9
     it a contingency.
             DR. LEWIS: Okay. Thank you, Dr. Crowley.
10
             Mr. Conway?
11
             MR. CONWAY:
                          Sure. Thank you very much.
12
             I think there could be efficacy. Again, I
13
14
      kind of go back to the idea that the mitigation
     measures in modeling do not substitute for testing
15
     prior to approval. Having said that, I really do
16
     understand the patient burden and the patient need
17
18
     here -- it's palpable -- but I think that we need
19
     to see that, especially in regard to issues related
      to VAT and considering that this population, in
20
21
     particular, is highly vulnerable.
             I'd also like to echo the larger point that
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has been made about diversity in the trials. actually why at the front end of the conversation today, I brought up the issue about the African American population because I wanted to know from some of the nephrologists whether or not, based on the safety data they were looking at, this is something they would engage African American patients on in a clinical setting since they are such a huge part of the dialysis patient population and our membership, the American Association of Kidney Patients. I just don't think that it lines up with confidence on the safety side before you put this out in a postmarket study situation. Thank you. DR. LEWIS: Thank you, Mr. Conway. Dr. Thadhani? DR. THADHANI: Thank you, Dr. Lewis. Ravi Thadhani. Certainly the comments that have been made are absolutely critical. If we look at the primary analysis, I think, as was stated before for MACE on the OT-plus-7, the neutral effects, the main issue we're dealing with here is

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the thromboembolic events. 1 I do believe there is a strong association, 2 with the emphasis on association, between starting 3 4 hemoglobin and rate of rise with that particular complication, which in a monitored setting would 5 be, I would say, easier to manage unlike in the 6 previous discussion. Thank you. 7 Thank you. DR. LEWIS: 8 Dr. Merz? 9 DR. BAIREY MERZ: Thank you. 10 Noel Bairey Merz. I have to agree with 11 12 Ms. Alikhaani that the very low rate of testing in African Americans makes me concerned about safety 13 signals that could be different. I have a lot of 14 experience about clinical trials that did not 15 enroll enough women, and it is only 10-15 years 16 after FDA approval we find out that it's not safe 17 18 in women. There are important facts as well as 19 genetic differences. It's not a stand-alone, but it is a comment, and I wanted to support her 20 21 concern. DR. LEWIS: 22 Thank you.

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If there is no further discussion on this discussion question, we will now move on to question 6, which is a voting question, but I will summarize our discussion before we do that.

In principle, I think that, again, the committee is still hearing the voice of patients wanting an alternative, but remains concerned about the safety signal and the ability of just reducing the dose to resolve the issue of that safety signal, whether it may even be related to it or whether it would be feasible to actually conduct it in a postmarketing setting where the efficacy could be less and the retention in the roxadustat group could be even less, and make it more difficult to assess that in the way they proposed to do the postmarketing evaluation.

I think people do feel more comfortable that for the in-center patients, the mitigation modeling could be implemented more easily. But again, this is a very vulnerable population and, again, it was emphasized that it also has a insufficient data base in what is a very important population in the

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U.S., African American patients.

So I am now going to a voting question, question 6, and I'm going to turn it to Dr. Yu.

DR. YU: Hi, everyone. This is just a reminder, again, before we vote, question 6 is a voting question. Voting members will use the Adobe Connect platform to submit their votes for this meeting. After the chairperson has read the voting question into the record and all questions and discussion regarding the wording of the vote question is complete, the chairperson will announce that the voting will begin.

If you're a voting number, you'll be moved to a breakout room. A new display will appear where you can submit your vote. There will be no discussion in the breakout room. You should select the radio button that is the round circular button in the window that corresponds to your vote, yes, no, or abstain. You should not leave the "no vote" choice selected.

Please note that you do not need to submit or send your vote. Again, you need only to select

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the radio button that corresponds to your vote. 1 You will have the opportunity to change your vote 2 until the vote is announced as closed. Once all 3 voting members have selected their vote, I will 4 announce that the vote is closed. 5 Next, the vote results will be displayed on 6 I will read the vote results from the 7 the screen. screen into the record. Next, the chairperson will 8 go down the roster and each voting member will 9 state their name and their vote into the record. 10 You can also state the reason why you voted as you 11 did, if you want. However, you should also address 12 any subparts of the voting question. 13 14 Are there any questions about the voting process before we begin? 15 DR. PACKER: I have just a question. 16 nature of this question is for the general 17 18 treatment of adult patients on dialysis; is that 19 fair? DR. LEWIS: That is how I would interpret 20 21 the question. It's not for a subgroup. 22 Does anyone from the FDA want to confirm

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that interpretation? 1 DR. UNGER: This is Dr. Unger. Yes, it's 2 for a general population. We're not talking about 3 any subgroups. 4 Does that answer your question, Dr. Packer? 5 DR. PACKER: Yes, it does. Thank you. 6 7 DR. LEWIS: I'm going to read the question. Should roxadustat be approved for the 8 treatment of anemia due to CKD in adult patients on 9 dialysis? If not, provide your rationale, as well 10 as recommendations, for additional data and/or 11 analysis that would support a favorable 12 benefit-risk profile and approval of roxadustat. 13 14 Are there any further questions or issues about the wording of the question? 15 Dr. Parsa, your hand is up. 16 I was asking the same question 17 DR. PARSA: 18 that was just asked in terms of how does one put in 19 the contingency or subgroup for the reasons that I had raised before, in terms of does one have to 20 21 vote for the population as a whole or do we just keep that as a remark afterwards if we have a 22

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      contingency for the subgroup, for example, the
     hyporesponsive?
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                          I think it's the latter, that
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             DR. LEWIS:
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      you would leave it as a comment when you explain
     your vote. Dr. Unger has made it clear that it's
5
      the population as a whole.
6
             If there are no further questions or
7
     comments concerning the wording of the question, we
8
     will now begin the voting on question 6.
9
                      Okay. We'll now move voting
10
             DR. YU:
      numbers into the voting breakout room to vote only.
11
      There will be no discussion in the voting breakout
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      room.
13
14
              (Voting.)
             DR. YU: The voting has closed and is now
15
     complete. Once the vote results display, I will
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      read the vote result into the record.
17
18
              (Pause.)
19
             DR. YU: The vote results are now displayed.
      I will read the vote totals into the record.
20
21
      chairperson will go down the list and each voting
     member will state their name and their vote into
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the record. You can also state the reason why you 1 voted as you did, if you want to. However, you 2 3 should also address any subparts of the voting question. 4 The vote total is 2 yeses, 12 noes, and zero 5 abstentions. Thank you. 6 7 DR. LEWIS: Thank you, Dr. Yu. We will now go down the list and have 8 everyone who voted state their name and vote into 9 the record. You may also provide justification for 10 your vote, if you wish to. However, please 11 12 remember to address any of the subparts of the question that corresponds to your vote. 13 We'll start with Dr. O'Connor. 14 DR. O'CONNOR: Christopher O'Connor. 15 Му vote was no. First, I want to thank the patient, 16 sponsor, and the FDA who participated in this 17 18 development program in really bringing a robust 19 program to the committee, which allowed us to do our job to protect public safety in a more robust 20 21 fashion with the large number of patients and events. 22

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As with the NDD, I'm concerned about the 1 adverse safety signal in the DD population, 2 particularly OS mortality given the high baseline 3 mortality and the absolute mortality risk. I don't 4 believe the modeling and mitigation strategy can 5 replace a prospective randomized trial, but I agree 6 with Dr. Packer, Dr. Lewis, and others that 7 exploring the current database to look at epo 8 resistance group as a possible narrow indication 9 10 link to a post-approval, randomized trial as the lower dose could be a path forward. Thank you. 11 12 DR. LEWIS: Thank you, Dr. O'Connor. Dr. Crowley? 13 14 DR. CROWLEY: Susan Crowley. I voted yes. I voted that based on, again, lack of the attrition 15 The primary analysis suggested neutrality 16 for both MACE as well as all-cause mortality. 17 18 Because there is an unmet need for our home 19 dialysis patients, as well as our epo-resistant patients, and I think that we have more control in 20 21 a dialysis setting for regulating dosing, et cetera. 22

doing this.

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              DR. LEWIS:
                          Thank you, Dr. Crowley.
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              Dr. Cook?
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              DR. COOK:
                        Thomas Cook. I voted no,
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     principally because I think we need more
      information on both the efficacy and safety of the
5
      dosing strategy.
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              DR. LEWIS:
7
                          Thank you.
              Dr. Kasper?
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                          Dr. Ed Kasper. Dr. Lewis,
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              DR. KASPER:
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      thank you very much; interesting day.
              I voted no, and Dr. O'Connor I think nicely
11
      summarized my reasonings as well. I would say that
12
13
      if the FDA wish to go forward with approval for
      roxadustat in ESA-resistant patients, that I would
14
      support that. Thank you.
15
                          Thank you, Dr. Kasper.
              DR. LEWIS:
16
              Dr. Packer?
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18
              (No response.)
19
              DR. LEWIS: Dr. Packer, you're probably
      still muted.
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              DR. PACKER: Julia, I'm so sorry. I keep
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This is Milton Packer. I voted no. I think there are real concerns about the safety in this population. Particularly, these are safety signals compared with a drug that already has defined safety risks. The real interesting opportunity here is a randomized trial of epo and roxadustat in people who are epo resistant. The real wonderful opportunity here is that the sponsor could actually test its lower dosing strategy so that there is an increase in hemoglobin compared to epo because these are epo-resistant patients. They could even show that the improvement in hemoglobin results in improvement in quality of life or other benefits that one would expect with an improvement in hemoglobin, and it would so straightforward to then assess benefit to risk in a defined patient population. So the epo-resistant group seems to be a real potential for future research. DR. LEWIS: Thank you, Dr. Packer. Dr. Wang?

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DR. WANG? Yes. This is Thomas Wang. I
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     voted no. I just want to say, despite my no votes
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     on both of the voting questions, this was a
     challenging vote for me just because, again, lack
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     of a clear-cut signal in one direction or another.
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             I do appreciate the potential benefits of
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7
     this medication, as well as the unmet clinical
     need, especially for the ESA unresponsive patients.
8
     I also appreciate the potential benefits of this
9
     novel mechanism of action.
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             My hope is that the applicant is going to be
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      able to obtain further data regarding the benefits
12
      and the risks to provide reassurance about some of
13
      the concerns that have been raised so that this
14
     medication can move forward. Thank you.
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             DR. LEWIS:
                          Thank you, Dr. Wang.
16
             Dr. Thadhani?
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             DR. THADHANI: Thank you, Dr. Lewis.
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             Ravi Thadhani. I'm the only other person
      that voted yes, other than Dr. Crowley as noted.
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      Interestingly enough, the rationale is similar to
      Dr. Kasper's comment, Dr. O'Connor's comment, and
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Dr. Packer's comment, and that is with a very
1
     careful label in terms of those individuals that
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      are hyporesponsive, perhaps in lieu also of
3
      transfusion; but also going back to what
4
     Dr. Crowley said, the opportunity for individuals
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      on peritoneal dialysis. We didn't talk about that,
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7
     but there was certainly data on that.
             So there is a window, an aperture, that we
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9
     can take advantage of.
                              I also am convinced that
      the sponsor is committed to both the risk
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     mitigation strategies we've talked about, as well
11
     as a post-approval study perhaps in the context of
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      the hyporesponsiveness.
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14
             Thank you, Dr. Lewis.
             DR. LEWIS: Thank you, Dr. Thadhani.
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             Mr. Conway?
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              (No response.)
18
             DR. LEWIS: Mr. Conway?
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             MR. CONWAY: Yes. My apologies.
      Conway. I voted no; again, my issues with the
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      safety and the dosing for both NDD and DD. I think
     we're in an era where we're pushing forward for
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more transplantation, more home dialysis, more peritoneal dialysis, and I think that the patient burden is real.

I think that the convenience could be better demonstrated, but I think you have to deal with this issue of the risk and of the safety, and make certain that's clear and upfront for the patient population and the patient consumers, who are ultimately the ones who are going to be looking for guidance from FDA on safety and from their medical professionals.

In regard to the conversations that have been had here about a potential path forward, at least for some populations, I agree. My caution would be make absolutely certain that that is representative of the dialysis population in the United States; and if it's not, I think you're going to have a hard time selling it if it's only coming from the nephrologists. I think it has to be the combination of FDA nephrologists and the sponsor putting patients upfront in the design of any type of trial. Thank you very much.

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Thank you, Mr. Conway.
              DR. LEWIS:
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              Dr. Cho?
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                        Leslie Cho. I voted no for many of
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              DR. CHO:
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      the reasons that have been stated before.
     concerned about the higher discontinuation rate of
5
      the roxadustat in this dialysis-dependent
6
     population when compared to epo. I am also
7
      concerned about the epo/hyporesponders.
8
              I am not convinced, given the data that's
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10
     been presented by the sponsor, that this particular
      drug would decrease, or would have equivalent
11
      thrombosis rate, or infection rate, or have less
12
     MACE or equivalent MACE. The lack of
13
14
      quality-of-life assessment in the epo/
     hyporesponders in this particular dialysis-
15
      dependent population is also a little bit
16
      concerning.
17
18
             Like Dr. Packer, I strongly urge the sponsor
19
     to do a study in the epo/hyporesponders since so
     much has been made about that particular
20
21
     population.
             DR. LEWIS:
22
                          Thank you.
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Ms. Alikhaani?

MS. ALIKHAANI: Yes. This is Jacqueline
Alikhaani. I voted no because the assessment of
the adverse events is just not altogether clear to
me. As we've been discussing all day today and all
the concerns that have been identified by other
members of the committee and others, a lot of
discrepancies that are really critical, and they
need to be addressed properly to be fair to the
patient who will be relying on this medication.

Those patients are putting their faith and their trust in all of us to get it right. So we have to do due diligence on every level to make sure we get things as best as we can and as correct as we can before we move forward.

As I mentioned before, I have family members living with this issue and some that have passed away, so it's also personal for me as well. I'm really just resonating with all the testimony of the patients who spoke to us today, and I think that we have to not let them down.

A lot of the testimony has just been very

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heartbreaking for me, and also the fact that we 1 can't move forward because of these discrepancies 2 on the safety issue. That's just as heartbreaking 3 for me because we need to do that before we can 4 help the patients the way they need to be helped. 5 Thank you. 6 7 DR. LEWIS: Thank you. Dr. Merz? 8 9 DR. BAIREY MERZ: Noel Bairey Merz. I voted no for the reasons stated. I think that these 10 safety concerns appear quite real. I don't think 11 12 FDA should approve on the basis of mitigation modeling. And because there is an alternate, we 13 14 should explore more how underserved the epo-resistant patients are, and I would use this 15 good hearing and this good information to start to 16 plan studies to understand that better. Thank you. 17 18 DR. LEWIS: Thank you, Dr. Bairey Merz. 19 This is Dr. Julia Lewis. I voted no. I voted no for many of the same reasons listed above. 20 21 However, I will also add that doing a study in the hyporesponsive patients would be a fantastic 22

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adjunct study, but I don't think it would be a 1 stand-alone study as a path to approval. 2 It's only 9-10 percent of our population, 3 maybe less. I think it's difficult to define in 4 some cases, and their safety profile may be 5 different than the general dialysis population or 6 certainly the non-dialysis population. So I think 7 that it could be done in addition but not in place 8 of a large, well-designed, efficient, 9 representative population study to better explore 10 the safety signals. 11 Dr. Moliterno? 12 DR. MOLITERNO: Thanks, Dr. Lewis. 13 14 David Moliterno, and I voted no. I've got a lot of notes, but others have already spoken to 15 I don't agree with all the comments from 16 everyone else, but that's ok. 17 18 I do think this drug has great potential. 19 Remember, this is the only oral agent that could potentially be available in the near term, so I 20 21 think that while I would love to see it for all dialysis-dependent patients as appropriate, I think 22

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that it's ok to get a side door, even if it's 1 10 percent of the population who may be epo or 2 3 other agent resistant. So I would encourage the sponsor to spend more time thinking about how to 4 get initial approval in them with secondary and 5 tertiary studies and continue to expand the label. 6 I look forward to seeing how the European 7 regulatory agency views the drug, and I look 8 9 forward to more data coming out of Asia as there's continued experience there. Thank you. 10 DR. LEWIS: Thank you, Dr. Moliterno. 11 Dr. Parsa? 12 DR. PARSA: Afshin Parsa, and I also voted 13 This is more of a conditional no since there 14 was really no mechanism for parsing out when yes 15 and when no, so I actually somewhat agree with 16 Dr. Thadhani and the yeses and the noes here. 17 18 At the end of the day, I think there's 19 potential and a good path here moving forward for the epo-resistant patients, but there certainly 20 21 doesn't seem to be much of a signal for the larger population, even if it's a weak [indiscernible] and 22

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somewhat consistent trend for increased risk with 1 otherwise not much benefit in the larger dialysis 2 population. 3 DR. LEWIS: Thank you, Dr. Parsa. 4 I will attempt to summarize this. I think 5 the two people who voted yes did so because they 6 felt that there was an unmet need, particularly for 7 home dialysis patients, and there was more control 8 over this population of patients, and the patients 9 and physicians involved would understand the risks. 10 There also was an interest in having a very 11 careful label perhaps for only hyporesponsive 12 patients and maybe home patients, and that would 13 give a doorway to a risk mitigation and 14 post-approval process as well. 15 I think the majority who had voted no are 16 still concerned about the adverse safety signal, 17 18 particularly the on-study mortality. I don't think 19 people are convinced that modeling supported by a phase 2 study can replace a clinical trial for 20 21 safety. I think there was a lot of interest in 22

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particularly studying the ESA-resistant patients 1 and maybe even a possible approval for them maybe 2 at a reduced dose, and maybe do a study with them. 3 But that did not substitute for, in some way, 4 examining the safety in the wider population. 5 I think people felt challenged by it. 6 think we all felt challenged by the unmet need for 7 alternatives in this population, but the safety 8 concerns outweighed the desire to help meet that 9 unmet need. 10 Before we adjourn, are there any last 11 comments from the FDA? 12 Dr. Unger? 13 14 DR. UNGER: Hi. Well, I would like to thank everyone who participated today in this challenging 15 application and this far-reaching discussion. I 16 thought it was excellent. I'd like to thank all of 17 18 you for your thoughtfulness, for your objectivity, 19 and I thank the people who have tried to follow the data and the science. Those are our guiding stars 20 21 at the FDA and I really appreciate that. I know this wasn't the vote that the 22

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applicant had hoped for, but I would like to credit
the applicant for running I think a very impressive
development program here. There wasn't always
agreement with the FDA, apparently, but
nevertheless, it was an impressive program. It's
the largest body of data we may ever see for a drug
like this, so I think a shout-out to them is in
order as well. And again, thank you to everyone.

Adjournment

DR. LEWIS: I would like to also thank everyone, but I specifically thought both the FDA and the sponsor gave us very, very well-written briefing documents, which very fairly and clearly presented the data. I do also appreciate the sponsor's quantity of data, which was also very helpful.

I want to thank all the speakers of the open hearing who joined us for sharing their time and thoughts with us. I want to thank the panel members. I want to thank particularly our patient and consumer reps for whom I know although this was hard -- obviously you could hear in everyone's

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voices more hard decisions, but probably
1
      particularly hard for both of you -- I thank both
2
      of you for your thoughtfulness in putting patients
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      first.
              I also want to mostly thank Dr. Joyce Yu,
5
      who really keeps me going here, for all her help
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7
      and support, and the rest of the FDA officers that
      make this meeting happen.
8
              We will now adjourn the meeting and, again,
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      thank you all.
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              (Whereupon, at 5:33 p.m., the meeting was
      adjourned.)
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EXHIBIT YY

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

		F orm 10-Q	
(Ma	ark One)		
V	QUARTERLY REPORT PURSUAN EXCHANGE ACT OF 1934	NT TO SECTION 13 OR	15(d) OF THE SECURITIES
	For the qu	arterly period ended June 30	, 2021
		OR	
	TRANSITION REPORT PURSUAN EXCHANGE ACT OF 1934	NT TO SECTION 13 OR	15(d) OF THE SECURITIES
	For the transition	on period fromto	
	Comn	nission file number: 001-3674	0
		ROGEN, IN of registrant as specified in its	
	Delaware		77-0357827
	(State or Other Jurisdiction of Incorporation or Organization)		(I.R.S. Employer Identification No.)
	409 Illinois Street		
	San Francisco , CA		94158
	(Address of Principal Executive Offices)	(44 5) 0 5 0 4000	(Zip Code)
	Registrant	(415) 978-1200 's telephone number, including area c	ode:
	Securities registered pursuant to Section 12		
	Title of each class	Trading Symbol	Name of each exchange on which
	Title of cueff chass	riuding Symbol	registered
	Common Stock, \$0.01 par value	FGEN	The Nasdaq Global Select Market
	Indicate by check mark whether the registran urities Exchange Act of 1934 during the preceding such reports), and (2) has been subject to such a subject to such the distance has also also also also also also also al	ing 12 months (or for such shor filing requirements for the past	ter period that the registrant was required to 90 days. Yes \square No \square
	Indicate by check mark whether the registran mitted pursuant to Rule 405 of Regulation S-T (ter period that the registrant was required to sul	(§ 232.405 of this chapter) duri	•
	Indicate by check mark whether the registran ller reporting company, or an emerging growth aller reporting company," and "emerging growth	company. See the definitions of	F"large accelerated filer," "accelerated filer,"
	Large accelerated filer ✓ Non-accelerated filer □		Accelerated filer □ Smaller reporting company □ Emerging growth company □

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition
period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the
Exchange Act.
Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2). Yes
No ☑
The number of shares of common stock outstanding as of July 31, 2021 was 92,621,941.

FIBROGEN, INC.

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ITEM 5. OTHER INFORMATION.

In a press release on April 6, 2021, the Company clarified that certain previously disclosed cardiovascular safety analyses from the roxadustat Phase 3 program for the treatment of anemia in chronic kidney disease included post-hoc changes to the stratification factors, and provided additional data from the cardiovascular safety analyses with the pre-specified stratification factors. As stated at that time, the Company initiated an internal review to ensure this does not occur in the future. We have now completed that review.

The Company's major findings are as follows:

- The underlying data used for cardiovascular safety analyses are accurate, with no data integrity issues with the data used to generate such analyses.
- In its NDA, the Company calculated accurately and described both sets of analyses, including the statistical methodologies and stratification factors utilized. The statistical analyses using post-hoc stratification factors were designated as "primary" analysis, and the statistical analyses using pre-specified stratification factors as a "sensitivity" analysis.
- We believe a number of elements contributed to the fact that the cardiovascular safety analyses designated as primary included post-hoc stratification factors. These include a complex data set with data from multiple clinical studies conducted by three companies, and a lack of clarity in the pooled cardiovascular safety analysis plans which identified multiple statistical methods and assessment periods.
- In addition, this information was compartmentalized within the organization, which relied on the founder and then-CEO to make key decisions and facilitate internal communication between groups. He unfortunately passed away in August 2019 prior to public disclosure of the detailed pooled safety analyses and the NDA filing.
- Those responsible for the statistical analyses believed that it was a reasonable and valid way to analyze and present the data.

Management is taking steps to ensure the Company's processes are consistent with best practices in all respects. We plan to implement and improve a number of processes and procedures, including independent quality unit oversight of clinical data management, programming, analysis, and reporting.

Those directly responsible for the decision to use post-hoc stratification factors in the primary analyses no longer work for the Company.

Exhibit 31.1

CERTIFICATION

- I, Enrique Conterno, certify that:
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 9, 2021 /s/ Enrique Conterno

Enrique Conterno Chief Executive Officer (Principal Executive Officer)

Exhibit 31.2

CERTIFICATION

- I, Pat Cotroneo, certify that:
- 1. I have reviewed this Form 10-Q of FibroGen, Inc.;
- 2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
- 3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
- 4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
- (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
- (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
- (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
- (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
- 5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
- (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: August 9, 2021 /s/ Pat Cotroneo

Pat Cotroneo

Senior Vice President, Finance and Chief Financial Officer

(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended ("Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Enrique Conterno, Chief Executive Officer of FibroGen, Inc. ("the Company"), and Pat Cotroneo, Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

- 1. The Company's Quarterly Report on Form 10-Q for the period ended June 30, 2021, to which this Certification is attached as Exhibit 32.1 ("Periodic Report") fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act, and
- 2. The information contained in the Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: August 9, 2021

IN WITNESS WHEREOF, the undersigned have set their hands hereto as of the 9 th day of August 2021.

/s/ Enrique Conterno	/s/ Pat Cotroneo
Enrique Conterno	Pat Cotroneo
Chief Executive Officer	Senior Vice President, Finance and
	Chief Financial Officer

This certification accompanies the Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of FibroGen, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

EXHIBIT ZZ





Press Release

Astellas Receives European Commission Approval for First-in-Class EVRENZO[™] (roxadustat) for Adult Patients with Symptomatic Anemia of Chronic Kidney Disease

Roxadustat is the first orally administered hypoxia-inducible factor (HIF) prolyl hydroxylase (PH) inhibitor available for adult patients with anemia associated with chronic kidney disease in Europe

TOKYO, August 20, 2021 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") and FibroGen, Inc. (Nasdaq: FGEN, CEO: Enrique Conterno, "FibroGen") today announced that the European Commission (EC) has approved EVRENZOTM (roxadustat) for the treatment of adult patients with symptomatic anemia associated with chronic kidney disease (CKD).

"We are very pleased EVRENZO has been approved as the first oral HIF-PH inhibitor to treat adult patients with symptomatic anemia associated with CKD in the European Union," said Steven Benner, M.D., M.H.S., President of Development, Astellas. "Today's approval provides patients, regardless of dialysis status, with a first-in-class treatment option to address the multifaceted nature of this condition. We look forward to making roxadustat available to adult patients with anemia of CKD in countries across the European Union."

CKD impacts one in 10 people globally, of whom one in five are affected by anemia. 1, 2 Anemia of CKD is often untreated or not treated to target, and is associated with reduced quality of life and progression to adverse cardiovascular (CV) and renal outcomes. 3-5

"Anemia is a significant and early complication of CKD that occurs with greater frequency and impact as CKD worsens, affecting patients' day-to-day living, self-care and mobility," said Jonathan Barratt, Ph.D., FRCP, Consultant Nephrologist and the Mayer Professor of Renal Medicine at the University of Leicester, United Kingdom. "This approval represents a step forward in providing patients with an efficient and simple option to manage anemia symptoms and maintain target hemoglobin levels to minimize the impact on their quality of life."

Roxadustat is the first orally administered HIF-PH inhibitor available in the European Union. Roxadustat increases hemoglobin (Hb) levels through a different mechanism of action compared to injectable erythropoiesis-stimulating agents (ESAs) which are typically co-administered with intravenous iron. As a HIF-PH inhibitor, roxadustat activates the body's natural response to reduced oxygen levels in the blood. This response involves the regulation of multiple, coordinated processes that allow management of anemia with a reduced use of intravenous iron.

"HIF-PH inhibitors represent a major advance in the treatment of anemia of CKD," said Mark Eisner, M.D., M.P.H., Chief Medical Officer, FibroGen. "Roxadustat provides a novel breakthrough for patients who suffer from this condition."

This approval follows the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) positive opinion to authorize roxadustat in June⁶ based on results from a comprehensive pivotal Phase 3 program comprising of eight multicenter and randomized studies, which involved 9,600 patients worldwide.⁷⁻¹² The results of this program showed roxadustat was efficacious in achieving and maintaining target Hb levels (10-12g/dL) in patients with symptomatic anemia of CKD regardless of dialysis status and irrespective of prior ESA treatment.⁷⁻¹¹ The safety profile observed in the roxadustat development program is reflective of the CKD populations studied and comparable to ESAs.⁷⁻¹²

The EC has the authority to approve medicines for European Union member states, as well as in the European Economic Area (EEA) countries Iceland, Norway, Liechtenstein.¹³

The EC approval of roxadustat triggers a milestone payment of \$120 million by Astellas to FibroGen, and FibroGen will also receive royalties based upon European net sales.

About CKD and Anemia of CKD

Chronic kidney disease (CKD) is a progressive disease characterized by gradual loss of kidney function that may eventually lead to kidney failure or end-stage renal disease, requiring dialysis or kidney transplant.¹⁴ Many patients with CKD die of cardiovascular complications before progressing to kidney failure and as such the prevalence of early kidney disease is much greater than end-stage disease.^{14, 15} CKD impacts one in 10 people globally and is predicted to become the fifth most common cause of premature death globally by 2040.^{1, 16}

Anemia, a serious medical condition in which patients have insufficient red blood cells and low levels of hemoglobin, is a common early complication of CKD affecting approximately 20% of CKD patients.^{2, 17} Anemia of CKD is associated with an increased risk of hospitalization, cardiovascular complications and death, and can also cause significant fatigue, cognitive dysfunction and reduced quality of life.^{4, 18} Blood transfusions are used for treating severe anemia, however, they may reduce a patient's opportunity for kidney transplant and can increase the risk of infection and/or complications such as heart failure and allergic reactions.^{19, 20}

About Roxadustat

Roxadustat, an oral medicine, is the first in a new class of medicines, HIF-PH inhibitors, that promote erythropoiesis, or red blood cell production, through increased endogenous production of erythropoietin; improved iron absorption and mobilization; and downregulation of hepcidin. Roxadustat is also in Phase 3 clinical development for anemia associated with myelodysplastic syndromes (MDS) and Phase 2 for chemotherapy-induced anemia (CIA).

Roxadustat is approved in EU member states, including the EEA countries, as well as in Japan, China, Chile and South Korea for the treatment of anemia of CKD in adult patients on dialysis (DD) and not on dialysis (NDD). Several other licensing applications for roxadustat have been submitted by Astellas and AstraZeneca to regulatory authorities across the globe and are currently in review.

Astellas and FibroGen are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia of CKD in territories including Japan, Europe, Turkey, Russia and the Commonwealth of Independent States, the Middle East, and South Africa. FibroGen and AstraZeneca are collaborating on the development and commercialization of roxadustat for the potential treatment of anemia of CKD in the U.S., China, other markets in the Americas, in Australia/New Zealand, and Southeast Asia.

Important Safety Information

The full European Summary of Product Characteristics (SPC/SmPC) for roxadustat will be available from the European Medicines Agency at www.ema.europa.eu ²¹

About Astellas

Astellas Pharma Inc., is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at https://www.astellas.com/en.

About FibroGen

FibroGen, Inc. is a biopharmaceutical company committed to discovering, developing and commercializing a pipeline of first-in-class therapeutics. The Company applies its pioneering expertise in hypoxia-inducible factor (HIF) and connective tissue growth factor (CTGF) biology to advance innovative medicines for the treatment of unmet needs. The Company is currently developing and commercializing roxadustat, an oral small molecule inhibitor of HIF prolyl hydroxylase activity, for anemia associated with chronic kidney disease (CKD). Roxadustat is also in clinical development for anemia associated with myelodysplastic syndromes (MDS) and for chemotherapy-induced anemia (CIA). Pamrevlumab, an anti-CTGF human monoclonal antibody, is in clinical development for the treatment of locally advanced unresectable pancreatic cancer (LAPC), Duchenne muscular dystrophy (DMD), and idiopathic pulmonary fibrosis (IPF). For more information, please visit www.fibrogen.com.

Astellas Cautionary Notes

In this press release, statements made with respect to current plans, estimates, strategies and beliefs, and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets and (vi) infringements of Astellas' intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development) that is included in this press release is not intended to constitute an advertisement or medical advice.

FibroGen Forward-Looking Statements

This release contains forward-looking statements regarding our strategy, future plans and prospects, including statements regarding the development and commercialization of the Company's product candidates, the prevalence of CKD and anemia, the potential safety and efficacy profile of our product candidates, our clinical and regulatory events. These forward-looking statements include, but are not limited to, statements about our plans, objectives, representations and contentions and are not historical facts and typically are identified by use of terms such as "may", "will", "should", "on track", "could", "expect", "plan", "anticipate", "believe", "estimate", "predict", "potential", "continue" and similar words, although some forward-looking statements are expressed differently. Our actual results may differ materially from those indicated in these forward-looking statements due to risks and uncertainties related to continued progress and timing of our various programs, including the enrollment and results from ongoing and potential future clinical trials, and other matters that are described in our Annual Report on Form 10-K for the fiscal year that ended December 31, 2020 and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2021 filed with the Securities and Exchange Commission (SEC), including the risk factors set forth therein. Investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date of this release, and we undertake no obligation to update any forward-looking statement in this press release, except as required by law.

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Contacts for inquiries or additional information:

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Astellas Pharma Inc. Corporate Advocacy & Relations TEL: +81-3-3244-3201

FibroGen, Inc. Investors: Michael Tung, M.D. Corporate Strategy / Investor Relations mtung@fibrogen.com Media: GCI Health FibroGenMedia@gcihealth.com

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EXHIBIT AAA

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

heck this box if no longer subject to Section 16. Form
or Form 5 obligations may continue. See Instruction
h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL OMB Number: 3235-0287 Expires: December 31, 2014 Estimated average burden hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* Yu K Peony						2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]									Person(s)	to Issuer	10% Owr	nor.
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o 05/16/20		nsaction (Mor	nth/Day/Y	(ear)		X	Director Officer (give tit	e below) Chief Me	edical O	Other (sp	ecify below)		
409 ILLINOIS ST.						ndment, Dat	e of Original	Filed (Mo	onth/Day	//Year)			6. Individ	ual or Joint/Group Form filed by 0	ne Repor	ting Pers	son	
(Street) SAN FRANCISCO	CA	94	158											Form filed by M	fore than (One Rep	orting Person	
(City)	(State)	(Z	ip)															
			T	able I -	Non-Der	ivative Se	curities A	cquirec	d, Dis _l	posed of	f, or Bene	eficially Ov	/ned					
1. Title of Security (Instr. 3)										ities Acquire , 4 and 5)	d (A) or Dispos		5. Amount of Secur Beneficially Owned		Direct (ership Form: D) or Indirect	7. Nature of Indirect Beneficial	
					(MONth/Day		th/Day/Voor)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)		(I) (Instr. 4)		Ownership (Instr. 4)
Common Stock					05/20/2	016		S		6,	107(1)	D	\$17.6 ⁽²⁾	214,011(3)		D	
				Table I			rities Acq , warrants		-			cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of Derivative Price of Derivative Security (Instr. 3) 3. Transaction Date Execution Date, if any (Month/Day/Year)						5. Number of Derivative Securities Acquired (A) Disposed of (D) (Instr. : 4 and 5)			6. Date Exercisable a Expiration Date (Month/Day/Year)			I Amount of Se Security (Instr.	curities Underlyi 3 and 4)	Derivative de Security (Instr. 5)		ber of ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
Security Code						V (A) (D)		Date Expiration Exercisable Date Title			Amount or Number of Shares	ount or mber of			Owned Following Reported Transaction(s) (Instr. 4)			

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$17.34 to \$17.96. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. Includes 1,389 shares purchased through the issuer's employee stock purchase plan on May 13, 2016.

Remarks:

/s/ Melissa Leon, Attorney-in-fact

05/18/2016 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

** Signature of Reporting Person

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

7	Check this box if no longer subject to Section 16. Form
ı	4 or Form 5 obligations may continue. See Instruction
	1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* Yu K Peony															of Reporting Pe cable) ector	erson(s) t	to Issuer	10% Owr	er
(Last)	(First)	(M	liddle)		3. Date o		nsaction (Mor	ear)			X	Officer (give title below) Ot Chief Medical Officer				Other (sp	er (specify below)		
C/O FIBROGEN, INC. 409 ILLINOIS ST.						ndment, Dat	e of Original I	Filed (Mon	nth/Day	/Year)			6. Individ	For	Joint/Group Fi rm filed by On	e Reporti	ing Pers	ion	
(Street) SAN FRANCISCO	CA		158											For	rm filed by Mo	re than C	One Rep	orting Person	
(City) (State) (Zip)						Ion-Derivative Securities Acquired, Disposed of, or Beneficially Owned													
1. Title of Security (Instr. 3)					Date Execution Date,					ities Acquire 4 and 5)	d (A) or Dispos		Benefic	ount of Securiti		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial	
					(MONth/Day		Ala/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)					Ownership (Instr. 4)
Common Stock					06/01/2	016		F		1,4	410 ⁽¹⁾	D	\$18.89		212,601			D	
				Table I			ırities Acq s, warrants					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative acquired (A) or f (D) (Instr. 3,	6. Date Expirati (Month/	tion Dat			Title and Amount of Securitie Privative Security (Instr. 3 and		J D	. Price of Perivative Security (Instr.)	9. Numb derivativ Securitie Benefici Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Followin Reporte Transact (Instr. 4)	tion(s)					

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

06/03/2016

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

Check this box if no longer subject to Section 16. Form

4 or Form 5 obligations may continue. See Instruction

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMEN

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden
hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* Yu K Peony						Name and Ti OGEN INC		5. Relation	ll appli	ip of Reporting Person(s) to l oplicable) Director			ssuer 10% Owner						
(Last)	(First)	(M	iddle)		3. Date o 06/10/20		nsaction (Mor	ear)			X	Chief Medical Officer Chief Medical Officer				Other (sp	(specify below)		
C/O FIBROGEN, INC. 409 ILLINOIS ST.		4. If Ame	ndment, Dat	e of Original	iled (Mon	nth/Day	/Year)			6. Individ	Fo	Joint/Group Form filed by On	e Reporti	ing Pers	son				
(Street) SAN FRANCISCO	CA		158											Fo	orm filed by Mo	re than C	one Rep	orting Person	
(City)	(State)	(Zi		Table I -	Non-Der	ivative Se	curities A	cquired	l, Disp	oosed of	f, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)							3. Transac Code (Inst		4. Securi		d (A) or Dispos	ed Of (D)	Benefi	ount of Securiti		Direct (ership Form: (D) or Indirect	7. Nature of Indirect Beneficial	
					(MONth/Day		Ala/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)			(i) (instr. 4)		Ownership (Instr. 4)
Common Stock					06/10/2	016		S		2,3	344(1)	D	\$17.96		210,257			D	
				Table I			irities Acq s, warrants		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative acquired (A) or f (D) (Instr. 3,	6. Date Expirati (Month/	tion Dat			I Amount of Se Security (Instr.	curities Underlyi 3 and 4)	S	Derivative Security (Instr. 5)		es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)			
Derivative Security Code						(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Owned Followin Reporte Transac (Instr. 4)	d tion(s)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/14/2016

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Reporting Person* Yu K Peony													5. Relation (Check a	II app		erson(s) to Issuer		10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)			3. Date of Earliest Transaction (Month/Day/Year) 09/01/2016								0	fficer (give title		edical O		ecify below)
409 ILLINOIS ST.					4. If Amendment, Date of Original Filed (Month/Day/Year)									Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person					
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158											F	orm filed by Mo	re than (One Rep	orting Person	
					Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned						vned								
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Year) 2. Deemed Execution Date, if any		3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispo	sed Of (D)	5. Amount of Securi Beneficially Owned Following Reported		Direct		ership Form: D) or Indirect	7. Nature of Indirect Beneficial	
					(MOIIII/Da)		th/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)		3 and	(I) (Instr. 4)		Ownership (Instr. 4)
Common Stock					09/01/2	016		F		1,4	410 ⁽¹⁾	D	\$17.33		208,847			D	
				Table I			irities Acc s, warrants					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	Derivative Security 2. Conversion or Exercise Price of Derivative Price of Derivative Price of Derivative Security (Month/Day/Year) 2. (Month/Day/Year) 3. Transaction Date Execution Date (Instr. 8) 4. Transaction Code (Instr. 8) 4. Transaction Code Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Security (Instr. 8)											9. Number of derivative Securities Beneficially Owned		10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.				
Security Code						(A) (D)		Date Exercis	Date Expiration		n Nu		Amount or Number of Shares				ng ed etion(s)		- ',

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

09/02/2016

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]						cker or Tradir	ig Symbol					5. Relation (Check a	II appli	of Reporting Pe icable) rector	erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		nsaction (Mor	nth/Day/Yea	ar)				X		ficer (give title	below) Chief Me	edical O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	iled (Monti	h/Day/	/Year)			6. Individ	Fo	Joint/Group Form filed by On	e Report	ing Pers	ion	
(Street) SAN FRANCISCO	CA	94	158											Fo	orm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi	ip)																
			T	able I -	Non-Der	ivative Se	curities A	cquired,	Disp	osed of	f, or Bene	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exec	ution Date,	3. Transacti Code (Instr.		4. Secur (Instr. 3,		d (A) or Dispos	ed Of (D)	Benef	ount of Securiti icially Owned wing Reported			ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOHUI/Day		th/Day/Voor)	Code	v	Amount		(A) or (D)	Price		action(s) (Instr.		(i) (ilisti	1. 4)	Ownership (Instr. 4)
Common Stock					09/14/2	016		S		2,3	345(1)	D	\$18.66		206,502			D	
				Table I		- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative equired (A) or f (D) (Instr. 3,	6. Date E Expiration (Month/D	on Dat	te		I Amount of Se Security (Instr.	curities Underlyi 3 and 4)	Ĭ [8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic	ve ies	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	Date Expiration 1							Amount or Number of Shares			Owned Following Reported Transaction(s) (Instr. 4)	ed ction(s)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/15/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ting Person*						cker or Tradir	ig Symbol					5. Relation	II applic	of Reporting Pecable)	erson(s) t	to Issuer	10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/01/20		nsaction (Mor	nth/Day/Yea	ar)				X		icer (give title	below) Chief Me	dical O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	iled (Mont	th/Day/	Year)			6. Individ		Joint/Group Fi m filed by On	• .		*	
(Street) SAN FRANCISCO	CA	94	158											For	m filed by Mo	re than (One Repo	orting Person	
(City)	(State)	(Z	p)		<u> </u>														
			Т	able I - I	Non-Deri	ivative Se	curities A	cquired,	Disp	osed of	, or Bene	ficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date	Exec	ution Date,	3. Transact Code (Instr		4. Securi		d (A) or Dispo	sed Of (D)	Benefic	unt of Securiti	es	Direct (I	rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		Ab/Dau/Vaan	Code	v	Amount		(A) or (D)	Price		ing Reported ction(s) (Instr.	3 and	(I) (Instr	. 4)	Ownership (Instr. 4)
Common Stock					12/01/2	016		F		1,4	410 ⁽¹⁾	D	\$20.55		209,792			D	
				Table I	- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed								
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative Acquired (A) or f (D) (Instr. 3,	6. Date I Expiration (Month/I	on Dat			Amount of Se Security (Instr	curities Underlyi 3 and 4)	De		9. Numb derivativ Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	Date Expiration N							Amount or Number of Shares			Owned Followin Reported Transact (Instr. 4)	tion(s)			

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

12/02/2016

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony				cker or Tradi	0 ,	ol			5. Relation (Check a	II app	of Reporting Pe licable) irector	erson(s)	to Issuer	10% Own	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/14/20		nsaction (Mo	nth/Day/Y	'ear)				X	0	fficer (give title		edical O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mo	onth/Day	/Year)			6. Individ		r Joint/Group Fi orm filed by On				
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158											F	orm filed by Mo	re than (One Rep	orting Person	
(Oily)	(Olulo)	(2)		able I - I	Non-Deri	ivative Se	curities A	cquired	d, Disp	posed of	, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	ution Date,	3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispo	sed Of (D)	5. Amount of Secu Beneficially Owner Following Reporte				ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MONTH/Day		th/Day/Year)	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (insti		Ownership (Instr. 4)
Common Stock					12/14/2	016		S		2,3	344 ⁽¹⁾	D	\$20.65		207,448			D	
				Table I			rities Acc s, warrants	•				cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	tion Code Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year)									ying 8. Price of Derivative Security (Instr. 5)		rivative derivat curity (Instr. Securit Benefic		10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	Date Expiration							Amount or Number of Shares	Foll Rep Tran		Owned Following Reported Transaction(s) (Instr. 4)		- ',		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/16/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ting Person*					Name and Tio		g Symbol				5. Relatio (Check a	ll appl	of Reporting Pelicable)	erson(s)	to Issuer	10% Owr	ner	
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 01/10/20	f Earliest Trai 17	nsaction (Mor	th/Day/Yea	ır)				X		fficer (give title	below) hief Me	dical O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Month	n/Day/`	Year)			6. Individ		Joint/Group Form filed by On	•		,	
(Street) SAN FRANCISCO	CA	94	158											Fo	orm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi	ip)																
			Т	able I -	Non-Deri	vative Se	curities A	quired,	Disp	osed of	, or Bene	ficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date	Execu		3. Transactio Code (Instr.		4. Securi (Instr. 3,		d (A) or Dispos	` ′	Benef	ount of Securiti	es	Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		h/Day/Year)	Code	,	Amount		(A) or (D)	Price		wing Reported action(s) (Instr.	3 and	(I) (Instr	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					01/10/2	017		S		5,0	000(1)	D	\$23.56 ⁽²⁾		202,448			D	
				Table I		- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) or (D) (Instr. 3,	6. Date E Expiratio (Month/D	n Date	•		Amount of Se Security (Instr	curities Underlyi . 3 and 4)	Ĭ	8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	Date Expiration N							Amount or Number of Shares	nt or er of		Followi Reporte	vned Illowing ported ansaction(s)		4)	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$23.10 to \$23.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

01/12/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trac		ol					ck all ap	nip of Reporting Poplicable)	erson(s) to	o Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/06/20		ransaction (M	onth/Day/Y	ear)						Officer (give title	,	dical Office	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, D	ate of Origina	l Filed (Mo	nth/Day	/Year)					or Joint/Group F Form filed by On	• (le Line)	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	re than Oi	ne Reporting	g Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative S	Securities /	Acquired	d, Disp	posed of	f, or Ben	eficially O	wned						
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day)	Ex	Deemed ecution Date,	3. Transac Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ber	Amount of Securiti neficially Owned lowing Reported	·	6. Ownership Direct (D) or (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(MONth/Day		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		(i) (instr. 4)		Ownership (Instr. 4)
Common Stock					03/06/20	017		F		4,7	727(1)	D	\$25.35		197,721		D		
Common Stock					03/08/20	017		A		41,	176(2)	A	\$0.00		238,897		D		
				Table I			curities Ac Ils, warran						ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	er of Derivative s Acquired (A) l of (D) (Instr. 3	or Expira	e Exerci tion Dat n/Day/Ye			d Amount of S Security (Inst		erlying	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficia Owned	re Forn es (D) o	Ownership n: Direct or Indirect nstr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerci:		Expiration Date	Title		Amount of Number of Shares			Followin Reported Transacti (Instr. 4)	d tion(s)		
Stock Option (Right to Buy)	\$25.4	03/08/2017		A		70,000		(3)	03/08/2027	Com	nmon Stock	70,0	00	\$0.00	70,00	00	D	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Represents the grant of restricted stock units. Twenty-five percent of the restricted stock units vest on March 6, 2018, and the remainder vests in equal amounts quarterly thereafter for the following three years.
- 3. Twenty-five percent of the shares subject to the option vests on March 1, 2018, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/08/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	ing Person*						cker or Tradi	0 ,	I				onship of Reporting F Il applicable) Director	erson(s) to	o Issuer	10% Own	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/14/20		nsaction (Mo	nth/Day/Ye	ear)				X	Officer (give title	e below) Chief Med	dical Of	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mor	nth/Day/	Year)			6. Individ	lual or Joint/Group F Form filed by Or	ne Reporti	ing Perso	on	
(Street) SAN FRANCISCO	CA	94	158										Form filed by Mo	ore than O	one Repo	orting Person		
(City)	(State)	(Zi	0)															
			Т	able I - I	Non-Deri	vative Se	curities A	Acquired, Disp		osed of	, or Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)							ution Date,	3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Securit Beneficially Owned		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect
					(Month/Day		Ab/Dau/Maan	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr 4)		(I) (Instr	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					03/14/20	017		S		4,6	551(1)	D	\$25.134(2)	234,246			D	
Common Stock					03/14/20	017		S		3,2	200(1)	D	\$25 .8 ⁽³⁾	25.8 ⁽³⁾ 231,046 D			D	
				Table I					equired, Disposed of, or Beneficially C ts, options, convertible securities)				ed	'				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative Acquired (A) of f (D) (Instr. 3,	r Expirat	Exercis ion Date /Day/Yea			I Amount of Se Security (Instr.	curities Underly 3 and 4)	ng 8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	Date Expiration V (A) (D) Exercisable Date Title Shares										Followir Reported Transact (Instr. 4)	d tion(s)	7)	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

- 2. The shares were sold at prices ranging from \$24.9125 to \$25.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$25.50 to \$26.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/16/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

** Signature of Reporting Person

Date

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trac		I					ionship of Reporting F all applicable)	Person(s) to	Issuer	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 04/25/20		Fransaction (M	onth/Day/Ye	ear)				X	Officer (give title	,		ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, D	ate of Origina	l Filed (Mor	nth/Day	/Year)			6. Indivi	dual or Joint/Group F Form filed by Or	• •	,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than On	ne Reporting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	vative S	Securities /	Acquired	l, Dis	osed of	, or Ben	eficially O	wned				
1. Title of Security (Instr. 3)								3. Transac Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	5. Amount of Securit Beneficially Owned Following Reported	0	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect Beneficial
					(MONth/Day		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr 4)		i) (ilistr. 4)	Ownership (Instr. 4)
Common Stock					04/25/20	017		M		5,	,000	A	\$14.575	236,046		D	
Common Stock					04/25/20	017		S		5,0	000(1)	D	\$28	231,046		D	
				Table I		Derivative Securities Ac (e.g., puts, calls, warrant							ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative s Acquired (A) d of (D) (Instr. 3	or Expirat	tion Dat			d Amount of S Security (Inst	ecurities Underly r. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficial Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Following Reported Transactio (Instr. 4)	ĭ	
Stock Option (Right to Buy)	\$14.575	04/25/2017		M			5,000	(2)		03/19/2024	Con	nmon Stock	5,000	\$0.00	107,00	00 D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

04/27/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

l	OMB APPROVAL	
	OMB Number:	3235-0287
	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	ing Person*						icker or Trad C [FGEN]	0 ,	ol				onship of Reporting F Il applicable) Director	erson(s) to	o Issuer	10% Own	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 05/10/20		ansaction (Mo	onth/Day/\	rear)				X	Officer (give title	below)	dical O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	te of Original	Filed (Mo	onth/Day	(Year)			6. Individ	lual or Joint/Group F Form filed by Or	ne Reporti	ing Pers	on	
(Street) SAN FRANCISCO	CA	94	158											Form filed by M	ore than O	One Repo	orting Person	
(City)	(State)	(Zi	p)															
			Т	able I - I	Non-Deri	vative Securities		cquire	d, Disp	osed of	f, or Bene	eficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact Date	Exec		3. Transa Code (In		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Securit Beneficially Owned		Direct (I	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		y ith/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr 4)		(I) (Instr	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					05/10/20	017		S		3,7	700(1)	D	\$26.17 ⁽²⁾	227,346			D	
Common Stock					05/10/20	017		S		1,3	300 ⁽¹⁾	D	\$26.97 ⁽³⁾	226,046			D	
				Table I			urities Ac s, warrant					cially Owne	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	of Derivative Acquired (A) of of (D) (Instr. 3	or Expir	e Exerci ation Dat h/Day/Ye			d Amount of Se Security (Instr.	curities Underly 3 and 4)	ng 8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerc		Expiration Date	Title	Amount or Number of Shares		Followin Reported	Owned Following Reported Transaction(s) (Instr. 4)	*)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

- 2. The shares were sold at prices ranging from \$25.65 to \$26.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$26.70 to \$27.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ John Alden, Attorney-in-fact

05/12/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

** Signature of Reporting Person

Date

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor			Name and Tion COMEN INC		g Symbol					nship of Reporting applicable) Director	Person(s)	to Issuer	10% Own	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/01/20	f Earliest Trar 17	nsaction (Mon	th/Day/Yea	ar)				X	Officer (give tit	e below) Chief Me	edical O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Montl	h/Day/	Year)			6. Individ	ual or Joint/Group Form filed by C	ne Repor	ting Pers	son	
(Street) SAN FRANCISCO	CA	94	158								Form filed by M	lore than	One Rep	orting Person				
(City)	(State)	(Zi		abla I I	Non Dori	vetive Sec	numition A	auiro d	Dian	anned of	i or Bono	oficially Ou	vnod					
1. Title of Security (Instr. 3)				able 1 - 1	Date Ex		eemed ition Date,	3. Transacti Code (Instr.	ion	1	ities Acquire	d (A) or Dispos	ed Of (D)	5. Amount of Secur Beneficially Owned		Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		h/Day/Voor)	Code	v	Amount		(A) or (D)		Following Reporte Transaction(s) (Inst 4)		(I) (Insti	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					06/01/2	017		F		1,4	410 ⁽¹⁾	D	\$27.6	226,057(2)		D	
				Table I		itive Secu outs, calls	•	-	•			cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	tion Code 5. Number of Derivative Securities Acquired (A) o Disposed of (D) (Instr. 3, 4 and 5)		6. Date E Expiration (Month/D	on Date	е		Amount of Se Security (Instr.	curities Underlyi 3 and 4)	8. Price of Derivative Security (Inst	Benefic	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)			Expiration Date Title			Amount or Number of Shares	Fol Rej Tra		Owned Following Reported Transaction(s) (Instr. 4)		, , , , , , , , , , , , , , , , , , ,

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 1,421 shares purchased through the issuer's employee stock purchase plan on May 15, 2017.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/02/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

Date

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person*				1		cker or Tradii	ng Symbol	I				5. Relation	ıll appli	of Reporting Policable)	erson(s) t	to Issuer	10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		nsaction (Mo	nth/Day/Ye	ear)				X		ficer (give title	below)	edical O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	e of Original	Filed (Mon	nth/Day	//Year)			6. Individ	Fo	Joint/Group F orm filed by On	e Report	ing Pers	ion	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	i-158												orm filed by Mo	ore than C	One Rep	orting Person	
			7	Γable I -	Non-Der	lon-Derivative Securities Acquired, Disposed of, or Beneficially Owned					/ned								
1. Title of Security (Instr. 3)					2. Transac Date	Exec	ution Date,	3. Transac Code (Inst			ities Acquire 4 and 5)	d (A) or Dispos	sed Of (D)	Benefi	ount of Securiti		Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		th/Day/Voor)	Code	v	Amount		(A) or (D)	Price		wing Reported action(s) (Instr.		(I) (Instr	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					06/06/2	2017		F		8	29(1)	D	\$29.05		225,228			D	
				Table I		- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)					ed								
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	ion Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securities Derivative Security (Instr. 3 and Date (Month/Day/Year)								S	8. Price of Derivative Security (Instr. 5) 9. Nun deriva Securi Benefi		ve ies	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	Date Expiration Nu							Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4)	ed ction(s)		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

06/08/2017 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]						cker or Tradir C [FGEN]	ng Symbol					5. Relation (Check a	II applic	of Reporting Pe cable) ector	erson(s) t	to Issuer	10% Owr	er
(Last)	(First)	(M	liddle)		3. Date o 06/14/20		insaction (Moi	nth/Day/Ye	ar)				X		icer (give title	below) hief Me	dical O	Other (sp	ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Da	e of Original	Filed (Mon	th/Day	/Year)			6. Individ	For	Joint/Group Fi rm filed by On	e Report	ing Pers	on	
(Street) SAN FRANCISCO	CA	94	158										For	rm filed by Mo	re than C	One Repo	orting Person		
(City)	(State)	(Zi	ip)																
			T	able I -	Non-Deri	on-Derivative Securities Acquired, Disposed of, or Beneficially Owned						ned							
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	ution Date,	3. Transact Code (Inst		4. Secur (Instr. 3,		d (A) or Dispos	ed Of (D)	Benefic	ount of Securiti			ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOnth/Day		th/Day/Voor)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Insti- 4)			(I) (IIIST	. 4)	Ownership (Instr. 4)
Common Stock					06/14/2	017		S		3,	721(1)	D	\$28.95	8.95 221,507				D	
				Table I		- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)					ed								
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	on Code 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 5. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securities Derivative Security (Instr. 3 and 5)								De	. Price of erivative ecurity (Instr.	9. Numb derivati Securiti Benefic Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	Date Expiration N							Amount or Number of Shares	lumber of		Followi Reporte Transac (Instr. 4)	tion(s)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

06/16/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony		FIBRO	Name and Tio	[FGEN]					all ap	ip of Reporting Poplicable) Director	erson(s)	to Issuer	10% Own	er					
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 07/10/20	f Earliest Trar 17	nsaction (Mor	th/Day/Yea	r))		Officer (give title	below) Chief Me	edical O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original I	Filed (Month	n/Day/`	Year)			6. Indi		or Joint/Group F Form filed by On			•	
	CA		158												Form filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi		able I - I	Non-Deri	vative Se	curities A	quired,	Disp	osed of	, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu		3. Transactio Code (Instr.		4. Securit (Instr. 3,		d (A) or Dispo	sed Of (D)	Ber	mount of Securiti eficially Owned owing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(WOITH/Day		h/Day/Year)	Code V	,	Amount		(A) or (D)	Price	T		3 and	(i) (ilisti	. 4)	Ownership (Instr. 4)
Common Stock					07/10/20	017		S		5,0	00(1)	D	\$32.98(2)		216,507			D	
				Table I		Derivative Securities Acquired, Disposed of, or Beneficially O (e.g., puts, calls, warrants, options, convertible securities)					-	ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A) or	6. Date Expiratio	n Date			I Amount of Se Security (Instr	ecurities Under . 3 and 4)	lying	8. Price of Derivative Security (Instr. 5)	9. Numl derivati Securiti Benefic	ve ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	Date Expiration Nu							Amount or Number of Shares	unt or ber of		Owned Following Reported Transaction(s) (Instr. 4)			- ',

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. The shares were sold at prices ranging from \$32.65 to \$33.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/11/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

** Signature of Reporting Person

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]						cker or Tradi	0 ,						5. Relation (Check al		,	rson(s) to	o Issuer	10% Own	er
(Last)	(First)	(M	iddle)		3. Date of 08/01/20		nsaction (Mo	nth/Day/Yea	r)					X		cer (give title l	below) hief Med	dical Of	Other (sp	ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Amer	ndment, Dat	e of Original	Filed (Month	n/Day/	Year)				6. Individ		oint/Group Fil n filed by One				
(Street) SAN FRANCISCO	CA	94	158												Form	n filed by Mor	e than O	ne Repo	orting Person	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	f, or Bene	eficially O	wned							
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec		3. Transaction Code (Instr.		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (´	Benefici	unt of Securitie ially Owned ng Reported			rship Form: 0) or Indirect	7. Nature of Indirect Beneficial
					(month/buy		th/Day/Year)	Code	′	Amount		(A) or (D)	Price	- 1		tion(s) (Instr. 3		(i) (iiioti.	")	Ownership (Instr. 4)
Common Stock					08/01/20	017		M		10),000	A	\$14	1.575		226,507			D	
Common Stock					08/01/20	017		S		10,	000(1)	D	\$33	.48(2)		216,507			D	
				Table I			irities Acc					icially Owr ties)	ned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative Acquired (A) of f (D) (Instr. 3,		n Date	•		d Amount of S Security (Inst			Dei	erivative curity (Instr.	9. Number derivative Securities Beneficial Owned	re I	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title			ount or ober of res			Followin Reported Transacti (Instr. 4)	d tion(s)		 ',
Stock Option (Right to Buy)	\$14.575	08/01/2017		M			10,000	(3)		03/19/2024	Com	mon Stock		10,000		\$0.00	97,00	00	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$33.45 to \$34.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/03/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep	orting Person*						cker or Trad	0 ,						tionship of Rep all applicable Director	e)	erson(s) to		10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 08/08/20		nsaction (Mo	onth/Day/Yea	ar)				X		(give title	,			ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Dat	e of Original	Filed (Mont	h/Day/`	Year)			6. Indiv		led by On	ne Reportin	g Person	,	
(Street) SAN FRANCISCO	CA	94	158											Form file	led by Mo	ore than Or	ne Reporting	Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	, or Ben	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day)	Exec		3. Transaction Code (Instr.		4. Securit (Instr. 3, 4		ed (A) or Dispose	d Of (D)	5. Amount of Beneficially Following R	y Owned	[6. Ownership Direct (D) or I (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(th/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction 4)			., (Ownership (Instr. 4)
Common Stock					08/08/20)17		М		20,	,000	A	\$14.575	2:	236,507		D		
Common Stock					08/08/20)17		S		32,4	100 ⁽¹⁾	D	\$50.5(2)	20	204,107		D		
Common Stock					08/08/20)17		S		5,1	00(1)	D	\$51.11(3)	19	199,007		D		
				Table I			ırities Ac	•	•			icially Owne	d						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative Acquired (A) of f (D) (Instr. 3		n Date	,		d Amount of Sec Security (Instr.		Deriva		9. Numbe derivative Securities Beneficia Owned	Form (D) or	wnership : Direct · Indirect str. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisa		expiration Date	Title		Amount or Number of Shares			Following Reported Transaction (Instr. 4)	ĭl		, i
Stock Option (Right to Buy)	\$14.575	08/08/2017		M			20,000	(4)	0	03/19/2024	Com	nmon Stock	20,000) \$(60.00	77,00	0	D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

- 2. The shares were sold at prices ranging from \$50.10 to \$50.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$51.00 to \$51.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Fully vested.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	ting Person [*]					Name and Ti OGEN INC		ng Symbol					5. Relati (Check a	all app	o of Reporting Policable)	erson(s)	to Issuer	10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o 08/21/20	f Earliest Tra 17	nsaction (Mo	nth/Day/Ye	ear)				X	С	Officer (give title		edical O	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mont	ith/Day	/Year)			6. Indivi		r Joint/Group F orm filed by On	٠.	• • •	,	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	1158 ip)											F	orm filed by Mo	ore than (One Repo	orting Person	
		<u> </u>		able I -	Non-Der	ivative Se	curities A	cquired,	, Disp	oosed of	f, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date	Exec	ution Date,	3. Transact Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	sed Of (D)	Bene	mount of Securiti	ies	Direct (I	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		h/Day/Voor)	Code	v	Amount		(A) or (D)	Price		owing Reported saction(s) (Instr.	3 and	(I) (Instr	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					08/21/2	017		S		7,5	500(1)	D	\$41.03 ⁽²⁾		191,507			D	
				Table I		ative Secu puts, calls						cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative acquired (A) of f (D) (Instr. 3,		ion Dat			d Amount of Se Security (Instr	curities Underly 3 and 4)	Ĭ	8. Price of Derivative Security (Instr. 5)	9. Numl derivati Securiti Benefic	ive ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)		4)

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$40.60 to \$41.275. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

08/23/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep Yu K Peony	orting Person*						Ticker or Trad	0 ,	ol					onship of Reporting all applicable) Director	Person(s) to		10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/01/20		ransaction (M	onth/Day/Y	ear)				X	Officer (give titl	,	dical Officer	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, D	ate of Origina	l Filed (Mo	nth/Day	//Year)			6. Indivi	dual or Joint/Group Form filed by C	• •		Line)	
(Street)														Form filed by M	ore than O	ne Reporting	Person	
SAN FRANCISCO	CA	94	158															
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative S	ecurities A	Acquire	d, Dis	posed of	f, or Bene	eficially Ov	ned					
1. Title of Security (Instr. 3)					2. Transact Date	Ex	. Deemed ecution Date,	3. Transa Code (Ins			ities Acquire 4 and 5)	d (A) or Dispos	ed Of (D)	5. Amount of Secur Beneficially Owned		6. Ownership Direct (D) or li		7. Nature of Indirect
					(Month/Day		iny onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Reporter Transaction(s) (Inst 4)		(I) (Instr. 4)		Beneficial Ownership (Instr. 4)
Common Stock					09/01/20	017		F		1,9	959(1)	D	\$49	189,548		D		
Common Stock					09/06/20	017		F		1,	151 ⁽¹⁾	D	\$48.1	188,397		D		
				Table I			curities Ac	. ,	•	,		cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	r of Derivative Acquired (A) of (D) (Instr. 3	or Expira	e Exerci ition Da n/Day/Ye			I Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr 5)	Beneficia	re Form: es (D) or	vnership Direct Indirect str. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exerci		Expiration Date	Title		Amount or Number of Shares		Owned Followin Reported Transacti (Instr. 4)	d ion(s)		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/06/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ting Person [*]				1		icker or Tradi C [FGEN]	0 ,	ol				5. Relatio (Check a			erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o		ansaction (Mo	nth/Day/Y	'ear)				X	Office	cer (give title	,	edical O	` '	ecify below)
409 ILLINOIS ST.					4. If Ame	endment, Da	te of Original	Filed (Mo	onth/Day	//Year)			6. Individ		oint/Group Fi n filed by One	• .		•	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158 p)											Form	n filed by Mo	re than (One Rep	orting Person	
			7	Table I -	Non-Der	ivative S	curities A	cquirec	d, Disp	posed of	f, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transac Date	Exe		3. Transac		4. Secur (Instr. 3,		ed (A) or Dispo		Beneficia	int of Securiti	es	Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		ng Reported tion(s) (Instr.	3 and	(I) (Instr	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					09/14/2	2017		S		2,	851(1)	D	\$51		185,546			D	
				Table I			urities Acc s, warrant		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) of of (D) (Instr. 3,	r Expira	e Exerciation Dat h/Day/Ye			d Amount of Se Security (Instr	curities Underlyi 3 and 4)	Der		9. Numb derivati Securiti Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerci		Expiration Date	Title		Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)		* ')

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/15/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep	porting Person*					Name and Tion		ng Symbol					ionship of Reporting F all applicable) Director	Person(s) to	lssuer 10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 10/02/201		nsaction (Mo	nth/Day/Year	1			X	Officer (give title	,	Other (sp	pecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	e of Original	Filed (Month/	Day/Year)			6. Indivi	•	ne Reportin	ng Person	
(Street) SAN FRANCISCO	CA	94	158										Form filed by M	ore than Or	ne Reporting Person	
(City)	(State)	(Zi	p)													
			Т	able I -	Non-Deri	vative Se	curities A	cquired, [ispose	d of, or Ben	neficially Ow	ned				
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day/	Execu	ition Date,	3. Transaction Code (Instr. 8		ecurities Acquir tr. 3, 4 and 5)	ed (A) or Dispos	ed Of (D)	5. Amount of Securi Beneficially Owned Following Reported	[6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
					,		h/Day/Year)	Code V	Amo	ount	(A) or (D)	Price	Transaction(s) (Instr 4)		,,,	Ownership (Instr. 4)
Common Stock					10/02/20	017		М		30,000	A	\$14.575	215,546		D	
Common Stock					10/02/20	017		S		11,000(1)	D	\$53.9(2)	204,546		D	
Common Stock					10/02/20	017		S		29,000(1)	D	\$54.9(3)	175,546		D	
				Table I				•	•	of, or Benef tible securi	ficially Own ities)	ed				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A) o		Date		nd Amount of Se e Security (Instr.		8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficia Owned	e Form: Direct (D) or Indirect	Indirect
	Security			Code	v	(A)	(D)	Date Exercisab	Expira e Date	tion Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)	i ion(s)	7,
Stock Option (Right to Buy)	\$14.575	10/02/2017		М			30,000	(4)	03/19/	2024 Cor	nmon Stock	30,000	\$0.00	47,00	00 D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

- 2. The shares were sold at prices ranging from \$53.20 to \$54.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$54.20 to \$55.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Fully vested.

Remarks:

10/04/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]			FIBRO	lame and Tio	[FGEN]	·25)			(Chec	k all ap	ip of Reporting Poplicable) Director	,	o Issuer	10% Own				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		10/04/201		isaction (ivid	лип/Дау/те	ai)					X (Officer (give title	below)	dical Off	` '	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	e of Original	Filed (Mon	th/Day	/Year)					or Joint/Group F Form filed by On	• (• • •	,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than O	ne Repo	rting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	, Disp	posed of	, or Bene	eficially O	wned						
1. Title of Security (Instr. 3)					Date E		Execution Date,				ties Acquire 4 and 5)	d (A) or Dispo	sed Of (D)	Ben	5. Amount of Securities Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(MOIIII/Day/		h/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		(i) (ilisti.	")	Ownership (Instr. 4)
Common Stock					10/04/20	017		M		15	5,000	A	\$14.575		190,546			D	
Common Stock					10/04/20)17		S		15,	000(1)	D	\$60		175,546			D	
				Table I		tive Secu outs, calls						cially Owr ies)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A)	r Expirati	ion Dat			d Amount of S Security (Inst	ecurities Unde r. 3 and 4)	derlying 8. Price of Derivative Security (Ins 5)		9. Number derivative Securitie Beneficia Owned	tive Form: Direct ties (D) or Indirect cially (I) (Instr. 4)		11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Followin Reported Transacti (Instr. 4)	ď		
Stock Option (Right to Buy)	\$14.575	10/04/2017		M			15,000	(2)		03/19/2024	Com	mon Stock	15,00	00	\$0.00	32,00	00	D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

10/06/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Case 3:21-cv-02623-EMC Document 111 Filed 01/14/22 Page 1389 of 1730

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ing Person*			Name and Tio		ng Symbol					nship of Reporting F I applicable) Director	Person(s) t	to Issuer	10% Own	or			
(Last)	(First)	(M	iddle)		3. Date of 11/06/20	Earliest Trar	nsaction (Mor	nth/Day/Yea	r)				X	Officer (give title	e below) Chief Me	dical O	Other (spe	ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original	Filed (Month	n/Day/Ye	ear)			6. Individ	ual or Joint/Group I Form filed by O	ne Reporti	ing Pers	on	
(Street) SAN FRANCISCO	CA	94	158											Form filed by M	ore than C	One Repo	orting Person	
(City)	(State)	(Zi	p)															
			able I -	Non-Deri	vative Sed	curities A	cquired,	Dispo	sed of	, or Bene	ficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transaction 2A. Deem Date Executio (Month/Day/Year) if any		ition Date,	3. Transactio Code (Instr.		4. Securit (Instr. 3,		d (A) or Dispos	` '	5. Amount of Securi Beneficially Owned		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect
					(Month/Day		h/Dau/Vaan\	Code V	,	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr 4)		(I) (Instr	·. 4)	Beneficial Ownership (Instr. 4)
Common Stock					11/06/20)17		S		5,4	42 ⁽¹⁾	D	\$55.16 ⁽²⁾	170,104		D		
Common Stock					11/06/20)17		S		2,0	058(1)	D	\$55.91 ⁽³⁾	168,046			D	
				Table I		Derivative Securities Acc (e.g., puts, calls, warrants				sposed of, or Beneficially Owned , convertible securities)			ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	tion Code Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Security (Instr. 3 and Derivative Security (Instr. 3 an									Derivative d Security (Instr. S 5) B		ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	Date Expiration Date Title										Owned Followin Reporte Transact (Instr. 4)	tion(s)		7)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

- 2. The shares were sold at prices ranging from \$54.70 to \$55.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$55.70 to \$56.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

11/08/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

** Signature of Reporting Person

Date

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	Name and Address of Reporting Person* 'u K Peony							Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] Date of Earliest Transaction (Month/Day/Year)										10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/01/20		nsaction (Mon	th/Day/Year	-)				X	0	fficer (give title	,	edical O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Month	/Day/\	Year)			6. Individ		r Joint/Group Fi orm filed by On	• .		•	
	CA (State)		158											F	orm filed by Mo	re than (One Rep	orting Person	
(Oily)							curities Ad	quired, [Disp	osed of	, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transaction Date 2A. Deemed Execution Date, (Month/Day/Year)			i. Transactio Code (Instr.		4. Securit		d (A) or Dispos	` ′	Bene	nount of Securiti ficially Owned wing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(WOIIII/Day		h/Dau/Vaan	Code V	,	Amount		(A) or (D)	Price	Transaction(s) (Instr. 3		3 and	(i) (iiisti	. 4)	Ownership (Instr. 4)
Common Stock					12/01/2	017		F		1,9) 58 ⁽¹⁾	D	\$47.15		166,088			D	
				Table I	- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)					ed									
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	saction Code Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount Expiration Date (Month/Day/Year)											9. Number of derivative Securities Beneficially		10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisab		Expiration Numb		Amount or Number of Shares	mber of		Owned Following Reported Transaction(s) (Instr. 4)			- ',	

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/05/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]				1		cker or Tradi	ng Symbo	ıl			5. Relation (Check a		,	erson(s) t	to Issuer	10% Owr	ier	
(Last)	(First)	(N	liddle)		3. Date of 12/06/20		nsaction (Mo	nth/Day/Ye	ear)				X	Offic	icer (give title	below) Chief Me	dical Of	` '	ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mor	nth/Day	//Year)			6. Individ	For	Joint/Group Fi rm filed by On	e Reporti	ing Perso	on	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Z	1158 ip)											Fori	rm filed by Mo	re than C	One Repo	orting Person	
			7	able I -	l Non-Der	ivative Se	curities A	cquired	l, Dis _l	posed of	f, or Bene	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transac Date	Execution Date,		3. Transac		4. Secur (Instr. 3,		d (A) or Dispos	sed Of (D)	Benefic	ount of Securiti cially Owned ring Reported		Direct (E	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		4h/Dau/Vaan	Code V		Amount		(A) or (D)	Price		isaction(s) (Instr. 3 and		(I) (Instr. 4)		Beneficial Ownership (Instr. 4)
Common Stock					12/06/2	017		F		1,	151(1)	D	\$44.85		164,937			D	
				Table I		- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Derivative Securities Acquired (A) Disposed of (D) (Instr. 3 4 and 5)			tion Da			I Amount of Se Security (Instr	curities Underlyi 3 and 4)	lying 8. Price of Derivative Security (Instr. 5)		9. Numb derivativ Securitie Benefici	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Owned Followin Reporte Transac (Instr. 4)	tion(s)		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

12/08/2017 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	Name and Address of Reporting Person* Vu K Peony							2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)										10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 12/14/20		nsaction (Mo	nth/Day/Ye	ear)				X	Of	ficer (give title		edical O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mor	nth/Day	/Year)			6. Individ		Joint/Group Fi orm filed by One			•	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158 									Fo	orm filed by Mo	re than (One Rep	orting Person			
	able I - I	Non-Deri	ivative Se	curities A	cquired	d, Disp	oosed of	, or Bene	ficially Ov	vned									
1. Title of Security (Instr. 3)								3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispo	sed Of (D)	Benef	ount of Securiti icially Owned wing Reported	es	Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		/ th/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr. 3		3 and	(I) (Instr	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					12/14/2	017		S		2,8	351 ⁽¹⁾	D	\$43.7		162,086			D	
				Table I				cquired, Disposed of, or Beneficiallynts, options, convertible securities)			•	ed	'						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative equired (A) o f (D) (Instr. 3,	r Expirat	Exercistion Dat ### Day/Year			Amount of Se Security (Instr	curities Underlyi . 3 and 4)	8. Price of Derivative Security (Instr. 5)		9. Num derivati Securiti Benefic Owned	tive Form: Direct (D) or Indirect (I) (Instr. 4)		11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	V (A) (D) Date Expiration Date Title								Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ing ed ction(s)		-,

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/15/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ting Person [*]				1		icker or Trad	ol				telationship of Reporting Pe eck all applicable) Director X Officer (give title		`,			10% Owner		
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o 01/29/20		ansaction (Mo	nth/Day/Y	(ear)				X	C	10	,	edical O	` '	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	te of Original	Filed (Mo	onth/Day	//Year)			6. Individ		r Joint/Group F form filed by On	•		•	
(Street) SAN FRANCISCO	CA		1158												orm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi		Table I -	Non-Derivative Securities Acqu		cquired	d, Disp	posed o	f, or Bene	eficially Ov	/ned							
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exe	Deemed cution Date,	3. Transac Code (Ins		4. Securi		d (A) or Dispos	ed Of (D)	Bene	mount of Securiti eficially Owned owing Reported	es		ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		y ith/Day/Year)	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (inst	r. 4)	Ownership (Instr. 4)
Common Stock					01/29/2	018		S		10,	,000(1)	D	\$62		152,086			D	
				Table I		Derivative Securities A (e.g., puts, calls, warrar			•		of, or Beneficially Owner		ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	sction Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securitie Derivative Security (Instr. 3 and Derivative Security											9. Num derivati Securit Benefic	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	Date Expiration N							Amount or Number of Shares			Owned Following Reporte Transac (Instr. 4	ing ed ction(s)		4)	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

01/31/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]				1		icker or Trad		ool				nship of Report I applicable) Director	ng Person(s	s) to Issue	r 10% Owr	nor	
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		ansaction (M	onth/Day/\	Year)				X	Officer (give	,) Medical C	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	ite of Origina	Filed (Mo	onth/Da	y/Year)			6. Individ	ual or Joint/Gro Form filed b	y One Repo	orting Pers	son	
(Street) SAN FRANCISCO	CA	94	158									Form filed b	y More thar	n One Rep	porting Person			
(City)	(State)	(Z	ip)															
			Т	able I -	Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned						/ned							
1. Title of Security (Instr. 3)					2. Transac Date	Exe	Deemed cution Date,	3. Transa Code (In		4. Secur (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Se Beneficially Ow	ned	Direct	ership Form: (D) or Indirect	7. Nature of Indirect
					(Month/Day		ny nth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr 4)			tr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					02/08/2	018		S		7,100 ⁽¹⁾ D		\$53.94(2)	144,986			D		
Common Stock					02/08/2	018		S		4	00(1)	D	\$54.51 ⁽³⁾	144,5	86		D	
				Table I	I - Derivative Securities Ac (e.g., puts, calls, warran								ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	of Derivative Acquired (A) of of (D) (Instr. 3	r Expir	te Exerc ration Da th/Day/Ye		te Derivative Security (Instr. 3 and			8. Price of Derivative Security (I 5)	deriva str. Secur Benef	ities ficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerc	cisable	Expiration Date	ation Nun		Amount or Number of Shares	Follo Repo Trans		Owned Following Reported Transaction(s) (Instr. 4)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

- 2. The shares were sold at prices ranging from \$53.40 to \$54.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$54.50 to \$54.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

02/09/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person*				1		icker or Tradi	ng Symbo	ol				5. Relati (Check	all app	o of Reporting Policable)	erson(s)	to Issuer	10% Owr	nor.	
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		ansaction (Mo	nth/Day/Ye	ear)				X		Officer (give title	below) Chief Me	edical O	Other (sp	ecify below)	
409 ILLINOIS ST.					4. If Ame	ndment, Da	te of Original	Filed (Mor	nth/Day	//Year)			6. Indivi	F	r Joint/Group F orm filed by On	e Report	ting Pers	ion		
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	i-158												orm filed by Mo	re than (One Rep	orting Person		
			7	Γable I -	Non-Der	on-Derivative Securities Acquired, Disposed of, or Beneficially Ow					ned									
1. Title of Security (Instr. 3)					2. Transac Date	Exe		3. Transac Code (Ins			ities Acquire , 4 and 5)	ed (A) or Dispo	sed Of (D)	Bene	nount of Securiti		Direct (ership Form: D) or Indirect	7. Nature of Indirect	
					(Month/Day		th/Day/Voor	Code	v	Amount		(A) or (D)	Price		owing Reported saction(s) (Instr.		(I) (Insti	r. 4)	Beneficial Ownership (Instr. 4)	
Common Stock					03/01/2	018		F		1,	297(1)	D	\$54.95		143,289			D		
				Table I						Derivative Securities Acquired, Disposed of, or Beneficially (e.g., puts, calls, warrants, options, convertible securities)				ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) o of (D) (Instr. 3,	r Expirat	6. Date Exercisable an Expiration Date (Month/Day/Year)			d Amount of Se Security (Instr	curities Underly 3 and 4)		Derivative de Security (Instr. 5)		ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	
	Security			Code	v	V (A) (D) Exercisable Expiration Date Title							Amount or Number of Shares	lumber of		Owned Following Reported Transaction (Instr. 4)	ing ed ction(s)	4)		

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

03/05/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony		1	Name and Tion OGEN INC		g Symbol					nship of Rep I applicable) Director		rson(s) to	Issuer	10% Own	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 03/06/20	f Earliest Trai	nsaction (Mor	th/Day/Yea	ar)				X	Officer (g		below) hief Med	lical Off	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original I	iled (Mont	th/Day/	(Year)			6. Individ	ual or Joint/0 Form file	d by One	Reportir	ng Persoi	n .	
(Street) SAN FRANCISCO	CA	94	158									Form file	ed by Mor	e than O	ne Repor	rting Person			
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Der	vative Se	curities A	quired,	Disp	osed of	, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transac	Exec	ıtion Date,	3. Transact Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	` ′	Beneficially (. Amount of Securities leneficially Owned following Reported		Direct (D)	ship Form:) or Indirect	7. Nature of Indirect
					(Month/Day		h/Dau/Vaan	Code	v	Amount	t (A) or (D) Price		Price	Transaction(s 4)			(I) (Instr.	4)	Beneficial Ownership (Instr. 4)
Common Stock					03/06/2	018		F		5,0	065(1)	D	\$53.55	13	8,224			D	
				Table I		Derivative Securities Acquired, Dis (e.g., puts, calls, warrants, options,			quired, Disposed of, or Beneficially Own s, options, convertible securities)			ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		f Derivative cquired (A) or (D) (Instr. 3,	6. Date E Expiration (Month/E	on Date			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	8. Price Derivati Security 5)	ive y (Instr.	9. Number derivative Securitie Beneficia	e F s (I	0. Ownership form: Direct D) or Indirect I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa	Date Expiration Exercisable Date		Expiration Num		Amount or Number of Shares			Followin Reported Transacti (Instr. 4)	ı		

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

03/08/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

l	OMB APPROVAL	
	OMB Number:	3235-0287
	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trac		ol					tionship of Reporti all applicable) Director	ng Person(s) to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/14/20		ransaction (M	onth/Day/Y	ear)				X		,	ledical Of	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amei	ndment, D	ate of Origina	l Filed (Mo	nth/Day	/Year)			6. Indiv	idual or Joint/Gro Form filed b		• • •	,	
(Street) SAN FRANCISCO	CA	94	158											Form filed b	/ More than	One Repo	orting Person	
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative S	ecurities A	Acquired	d, Disp	posed of	f, or Ben	eficially O	wned					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	Deemed ecution Date,	3. Transac Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	5. Amount of Se Beneficially Own Following Repo	ed		rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Day		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (I		(i) (ilisti	. 4)	Ownership (Instr. 4)
Common Stock					03/14/20	018		S ⁽¹⁾		9,	,891	D	\$53.2	128,3	33		D	
Common Stock					03/14/20	018		A		32,	000(2)	A	\$0.00	160,3	33		D	
				Table I			curities Ac						ned					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	r of Derivative Acquired (A) of (D) (Instr. 3	or Expira	Exerci tion Dat /Day/Ye			d Amount of S Security (Inst	ecurities Underl : 3 and 4)	ying 8. Price of Derivative Security (II 5)	deriva	tive ities icially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Follow Repor	ving ted action(s)		-,
Stock Option (Right to Buy)	\$53.75	03/14/2018		A		55,000		(3)	03/14/2028	Com	mon Stock	55,000	\$0.00	55	5,000	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Represents the grant of restricted stock units. Twenty-five percent of the restricted stock units vest on March 6, 2019, and the remainder vests in equal amounts quarterly thereafter for the following three years.
- 3. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

03/16/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	ing Person*			Name and Tio		ng Symbol					nship of Reporting F I applicable) Director	erson(s) to	o Issuer	10% Own	or			
(Last)	(First)	(M	iddle)		3. Date of 04/16/20	Earliest Trar	nsaction (Mor	nth/Day/Yea	ır)				X	Officer (give title	below)	dical Off	Other (spe	ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original	Filed (Month	n/Day/\	Year)			6. Individ	ual or Joint/Group F Form filed by Or	ne Reporti	ng Perso	on ,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than O	ine Repo	orting Person	
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	on-Derivative Securitie		cquired,	Disp	osed of	, or Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)					Date Exec			3. Transactio Code (Instr.		4. Securi (Instr. 3,		d (A) or Dispos	` '	5. Amount of Securit Beneficially Owned		Direct (D	rship Form:)) or Indirect	7. Nature of Indirect
					(Month/Day		n/Day/Year)	Code \	<i>,</i>	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)		nd (I) (Instr. 4)		Beneficial Ownership (Instr. 4)
Common Stock					04/16/20	018		S ⁽¹⁾		4,	,100	D	\$47.39(2)	156,233		D		
Common Stock					04/16/20	018		S ⁽¹⁾		3,	400	D	\$48.31(3)	152,833			D	
				Table I		tive Secu						cially Own es)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	tion Code Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 5. Number of Derivative Securities Acquired (A) or (Month/Day/Year) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Se Derivative Security (Instr. 4) (Month/Day/Year)								8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Beneficia Owned	e F	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	V (A) (D) Date Expiration Date Title St									Followin Reported Transact (Instr. 4)	d ion(s)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

- 2. The shares were sold at prices ranging from \$46.95 to \$47.75. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$48.00 to \$48.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

04/18/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor			Name and Tion COMENTING		g Symbol					nship of Reporting I applicable) Director	Person(s)) to Issuer	- 10% Own	er					
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/01/20	f Earliest Trar 18	nsaction (Mor	th/Day/Yea	ar)				X	Officer (give t	tle below) Chief M	ledical O		ecify below)	
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Mont	h/Day/	Year)			6. Individ	ual or Joint/Grou Form filed by	One Repo	rting Pers	son		
(Street) SAN FRANCISCO	CA	94	158								Form filed by	More than	One Rep	oorting Person					
(City)	(State)	(Zi																	
	Tab						curities A	quired,	Disp	osed of	, or Bene	ficially Ov	vned						
1. Title of Security (Instr. 3)					Date Execution Date,		3. Transacti Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	` ′	5. Amount of Sec Beneficially Owner Following Report	d		ership Form: D) or Indirect	7. Nature of Indirect Beneficial		
					(WORLII/Day		h/Doy/Voor)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (In 4)		(i) (inst	r. 4)	Ownership (Instr. 4)	
Common Stock					06/01/2	018		F		99	93(1)	D	\$54.05	153,260	2)		D		
				Table I		Derivative Securities Acq (e.g., puts, calls, warrants					•		ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number o Securities A Disposed of 4 and 5)	cquired (A) or	6. Date E Expiration (Month/D	on Date	е		Amount of Se Security (Instr	curities Underlyi 3 and 4)	8. Price of Derivative Security (Ins	Benefi	tive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.	
	Derivative Security			Code	v	(A)	(D)					Expiration Num		Amount or Number of Shares		Follow Repor Transa	Owned Following Reported Transaction(s) (Instr. 4)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 1,420 shares purchased on May 15, 2018 through the Issuer's ESPP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/05/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	iing Person [*]						cker or Tradi	0 ,	ol				5. Relation (Check a	II appli	of Reporting Pe icable) rector	erson(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/06/20		nsaction (Mo	nth/Day/Y	'ear)				X	Of	ficer (give title		edical O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mo	onth/Day	/Year)			6. Individ		Joint/Group Fi orm filed by On				
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158											Fo	orm filed by Mo	re than (One Rep	orting Person	
(4.3)	(*******)			able I - I	Non-Deri	ivative Se	curities A	cquired	d, Disp	posed of	, or Bene	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	ution Date,	3. Transac Code (Ins		4. Securi		d (A) or Dispo		Benef	ount of Securiti icially Owned wing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MORTH/Day		th/Day/Year)	Code	v	Amount		(A) or (D)			action(s) (Instr.	3 and	(i) (instr		Ownership (Instr. 4)
Common Stock					06/06/2	018		F		2,3	369 ⁽¹⁾	D	\$56.6		150,891			D	
				Table I			rities Acc s, warrants					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative acquired (A) o f (D) (Instr. 3,	r Expira	e Exercis ation Dat h/Day/Ye			I Amount of Se Security (Instr	curities Underlyi 3 and 4)	Ĭ E	3. Price of Derivative Security (Instr. 5)	9. Numl derivati Securiti Benefic Owned	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ing ed ction(s)		- ',

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

06/08/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

l	OMB APPROVAL	
	OMB Number:	3235-0287
	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Yu K Peony	ng Person [*]					Name and Tio		g Symbol					5. Relation (Check a	II app	of Reporting Pelicable) irector	erson(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/14/20	f Earliest Trar 18	nsaction (Mor	th/Day/Yea	-)				X	0	fficer (give title	,	dical Of	` '	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	Filed (Month	/Day/Y	ear)			6. Individ		r Joint/Group F orm filed by On	• .		•	
	CA (State)	94 (Zi	158 p)											F	orm filed by Mo	re than (One Repo	orting Person	
				able I - I	l Non-Deri	vative Sec	curities A	quired,	Dispo	sed of	, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transact	Execu	ution Date,	3. Transactio Code (Instr.		4. Securit (Instr. 3,		d (A) or Dispos		Bene	nount of Securiti	es	Direct (I	rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		h/Day/Voor)	Code	,	Amount		(A) or (D)	Price		wing Reported saction(s) (Instr.	3 and	(I) (Instr	. 4)	Ownership (Instr. 4)
Common Stock					06/14/2	018		S		3,4	22(1)	D	\$59.2		147,469			D	
				Table I		ntive Secu puts, calls		•	•			cially Own es)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities Ad Disposed of 4 and 5)	cquired (A) or	6. Date Expiratio	n Date			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	- I	8. Price of Derivative Security (Instr. 5)	9. Numi derivati Securiti Benefic Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisat		cpiration ate	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ed tion(s)		*)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

06/15/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	ing Person*				FIBRO	Name and Tid IGEN INC	[FGEN]								nship of Reporting P applicable) Director	erson(s) t	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 07/03/20		nsaction (Mo	nth/Day/Year)					X	Officer (give title	below)	dical Of		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original	Filed (Month/	/Day/\	(ear)				6. Individu <mark>X</mark>	al or Joint/Group F Form filed by On	ne Reporti	ing Perso	on	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mc	ore than C	One Repo	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	curities A	cquired, [Disp	osed of	, or Bene	eficially Ov	wned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu		3. Transaction Code (Instr. 8		4. Securit (Instr. 3,		d (A) or Dispo	sed Of (I	· E	5. Amount of Securit Beneficially Owned Following Reported			ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(монильау		h/Day/Year)	Code V		Amount		(A) or (D)	Price		Fransaction(s) (Instr.		(i) (iiisti	. 4)	Ownership (Instr. 4)
Common Stock					07/03/20	018		M		15	,645	A	\$14	1.575	163,114			D	
Common Stock					07/03/20	018		S		15,0	645(1)	D	\$	65	147,469			D	
				Table I				uired, Dis s, options				cially Owr ies)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A) o		Date			d Amount of So Security (Instr			g 8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisab		xpiration ate	Title			unt or ber of es		Followin Reporte Transact (Instr. 4)	tion(s)		, , , , , , , , , , , , , , , , , , ,
Stock Option (Right to Buy)	\$14.575	07/03/2018		М			15,645	(2)	0	3/19/2024	Com	mon Stock		15,645	\$0.00	16,3	355	D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

07/06/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]				FIBRO	<u>GEN</u>	d Ticker or Trad]						k all ap	p of Reporting Popularies plicable) Director	erson(s) to	Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 08/31/20		Transaction (M	onth/Day/Ye	ar)				2	X (Officer (give title	below) Chief Medi	ical Of	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Origina	Filed (Mon	th/Day	/Year)					or Joint/Group F Form filed by On	- 1		,	
(Street) SAN FRANCISCO	CA	94	158											F	Form filed by Mo	ore than On	ne Repo	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Der	ivative	Securities A	Acquired,	, Disp	osed of	, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		A. Deemed Execution Date, f any	3. Transact Code (Inst		4. Securi (Instr. 3,		ed (A) or Dispos	ed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	0		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(months buy		Month/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		i) (iii3ti .	. 4)	Ownership (Instr. 4)
Common Stock					08/31/2	018		М		1,	800	A	\$5.95	T	149,269			D	
Common Stock					08/31/2	018		M		5,	000	A	\$14.575		154,269			D	
Common Stock					09/04/2	018		F		99)4 (1)	D	\$61.05		153,275			D	
				Table I			ecurities Ac alls, warrant			,		•	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securit	ber of Derivative ies Acquired (A) o ed of (D) (Instr. 3)	or Expirati	on Dat			d Amount of Se Security (Instr.		rlying	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficial	e s	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercis	able	Expiration Date	Title		Amount or Number of Shares			Owned Following Reported Transactio (Instr. 4)	ĭ		4)
Stock Option (Right to Buy)	\$5.95	08/31/2018		M			1,800	(2)		06/27/2022	Com	mon Stock	1,800	0	\$0.00	0		D	
Stock Option (Right to Buy)	\$14.575	08/31/2018		M			5,000	(2)		03/19/2024	Com	mon Stock	5,000	0	\$0.00	11,35	5	D	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Fully vested.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ting Person [*]						cker or Tradir	ng Symbol					5. Relatio (Check a		,	erson(s) t	to Issuer	10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 09/06/20		nsaction (Mo	nth/Day/Ye	ear)				X		cer (give title	below) hief Me	dical O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mon	ith/Day/	Year)			6. Individ		Joint/Group Fi m filed by One	• .		*	
(Street) SAN FRANCISCO	CA	94	158											Fori	m filed by Mo	re than C	One Repo	orting Person	
(City)	(State)	(Z		able I	Non Dori	votivo So	ouritios A		Dian		i or Pone	ficially Ov	mad						
1. Title of Security (Instr. 3)			<u> </u>	ubic i -	2. Transact Date (Month/Day	tion 2A. E	eemed ution Date,	3. Transact	tion	1	ties Acquire	d (A) or Dispos	ed Of (D)	Benefic	unt of Securiticially Owned	es		rship Form: D) or Indirect	7. Nature of Indirect Beneficial
							th/Day/Vaan	Code	v	Amount		(A) or (D)	Price		ction(s) (Instr.	3 and	.,,		Ownership (Instr. 4)
Common Stock					09/06/2	018		F		2,3	368(1)	D	\$57.3		150,907			D	
				Table I			rities Acq s, warrants		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative equired (A) or f (D) (Instr. 3,		ion Dat			Amount of Se Security (Instr	curities Underlyii 3 and 4)	Ĭ De		9. Numb derivativ Securition Benefici Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Following Reporte Transac (Instr. 4)	tion(s)		4 ,

Explanation of Responses:

1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

09/06/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep	orting Person*						cker or Tradi	0 ,						onship of Reporting F all applicable) Director	erson(s) to	Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/03/201		nsaction (Mo	nth/Day/Yea	ır)				X	Officer (give title	,	Other (s	pecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Dat	e of Original	Filed (Month	n/Day/Y	Year)			6. Indivi	dual or Joint/Group F Form filed by O	• (,	
(Street)														Form filed by M	ore than On	ne Reporting Person	
SAN FRANCISCO	CA	94	158														
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Dispo	osed of	, or Bene	eficially Ow	ned				
1. Title of Security (Instr. 3)					2. Transacti Date	Exec		3. Transaction Code (Instr.		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Securi Beneficially Owned	0	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
					(Month/Day		y th/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr 4)		l) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					12/03/20	018		F		99	93(1)	D	\$43.93	149,914		D	
Common Stock					12/06/20	018		F		2,3	369 ⁽¹⁾	D	\$40.93	147,545		D	
				Table I			irities Acc		•	,		cially Own	ed				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)		Securities A	of Derivative acquired (A) of f (D) (Instr. 3,		n Date			I Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficial	Form: Direct (D) or Indirect	Indirect Beneficial Ownership (Instr
	Derivative Security			Code	v	(A)	(D)	Date Exercisal		xpiration ate	Title		Amount or Number of Shares		Owned Following Reported Transactio (Instr. 4)		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/06/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporti Yu K Peony	Name and Address of Reporting Person* Vu K Peony							g Symbol					onship of Reporting Il applicable) Director	Person(s)	to Issuer	10% Own	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/14/20	f Earliest Trar 18	nsaction (Mor	th/Day/Yea	ar)				X	Officer (give titl	,	edical Of	Other (specify below)	
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Mont	h/Day/`	Year)			6. Individ	lual or Joint/Group Form filed by C	٠,		,	
	CA (State)	94 (Zi	158											Form filed by M	ore than (One Repo	orting Person	
							curities A	quired,	Disp	osed of	, or Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)					Date Execution Date,			3. Transact Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Secur Beneficially Owned		Direct (D	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day/Year) if any (Month		h/Day/Voor)	Code V		Amount		(A) or (D)	Price	Following Reporte Transaction(s) (Inst 4)		(I) (Instr.	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					12/14/2018			s ⁽¹⁾ 3,422 D					\$38.58	144,123			D	
				Table I		itive Secu outs, calls			•	-		cially Own es)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) or (D) (Instr. 3,	6. Date E Expiration (Month/E	on Date			Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr	Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.		
	Code	v	(A) (D)		Date Expirat		xpiration ate	n Num		Amount or Number of Shares		Owned Following Reported Transactio (Instr. 4)	ed wing rted saction(s)		4)			

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/18/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep	orting Person*			FIBRO	GEN INC	cker or Tradi						onship of Reporting F all applicable) Director	Person(s) to	o Issuer 10% O	vner						
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/04/20		nsaction (Mo	nth/Day/Yea	ar)				X	Officer (give title	,	Other (specify below)				
409 ILLINOIS ST.					4. If Amer	ndment, Dat	e of Original	Filed (Monti	h/Day/	Year)			6. Indivi	dual or Joint/Group F Form filed by O	• (,					
(Street)													Form filed by M	ore than Or	ne Reporting Persor						
SAN FRANCISCO	CA	94	158																		
(City)	(State)	(Zi	p)																		
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	, or Bene	eficially Ow	ned								
1. Title of Security (Instr. 3)					Date	2. Transaction 2A. D Date Exec (Month/Day/Year) if any		3. Transacti Code (Instr.			ties Acquired (A) or Disposed Of 4 and 5)		ed Of (D)	5. Amount of Securi Beneficially Owned		6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect				
					(Month/Day		th/Day/Year)	Code	v	Amount	(A) or (D)		Price	Following Reported Transaction(s) (Instr 4)		(I) (Instr. 4)	Beneficial Ownership (Instr 4)				
Common Stock					03/04/20	019		F		69	93(1)	D	\$58.69	196,530		D					
Common Stock					03/06/2019			F		4,9	145 ⁽¹⁾	D	\$55.58	\$55.58 191,585 D							
				Table I			rities Acc		•	,		cially Own ies)	ed								
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative equired (A) of f (D) (Instr. 3,		on Date	е		I Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr. 5)	Beneficia	e Form: Direct s (D) or Indire	Indirect t Beneficial Ownership (Instr				
	Security Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Am Nui Title Sha			Foll Rep Trai	Owned Following Reported Transaction (Instr. 4)	ı	4)				

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

03/06/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony		1	Name and Ti OGEN INC		0 ,	I				onship of Repo Il applicable) Director	rting Pers	son(s) to I	Issuer 10% Ow	ner				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/14/20	f Earliest Tra 19	nsaction (Mo	nth/Day/Ye	ear)				X	Officer (g		,	Other (s	pecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mor	nth/Day/	/Year)			6. Individ	ual or Joint/G Form filed			k Applicable Line) g Person	
	CA (State)	94 (Zi _l	158 D)											Form filed	by More	than One	e Reporting Person	
			Т	able I - I	Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned						/ned							
1. Title of Security (Instr. 3)					Date Execution Date, if any (Month/Day/Year)		3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispos	sed Of (D)	5. Amount of Beneficially C	wned	Di	Ownership Form:	7. Nature of Indirect	
								Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Insti- 4)) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					03/14/2	019		S ⁽¹⁾		9	,145	D	\$56.3	182	,440		D	
				Table I		ative Secu puts, calls			•			cially Own es)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative equired (A) o f (D) (Instr. 3,	r Expirat	Exercis tion Date /Day/Yea			Amount of Se Security (Instr	curities Underly 3 and 4)	ying 8. Price of Derivative Security (Instr 5)		. Number lerivative securities seneficially	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr. 4)		
	Security			Code	v	(A)	(D)			Expiration Date	Title		Amount or Number of Shares		F R Ti	wned ollowing eported ransaction(s) nstr. 4)		**

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

03/15/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report			Name and Ti	cker or Tradir	ig Symbol					5. Relationship of Reportinç Check all applicable) Director		erson(s) t	to Issuer	10% Own	or.				
l` '	(First)	(M	liddle)		3. Date o 06/06/20		nsaction (Mor	nth/Day/Ye	ar)				X		er (give title	e below) Other (sp Chief Medical Officer			ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original	iled (Mon	th/Day	/Year)			6. Individ	, , ,					
	CA (State)	94 (Zi	158											Form	n filed by Mo	re than (One Repo	orting Person	
(City)	ahle I -	Non-Deri	ivative Se	curities A	rauired	Disr	no bean	f or Bene	eficially Ov	med									
1. Title of Security (Instr. 3)					2. Transac	Date Execution Date, C			tion r. 8)	_	ities Acquire	d (A) or Dispos	sed Of (D)	Beneficia	int of Securiti	es	Direct (I	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day/Year) if any (Month/Day/		th/Day/Vaan	Code	v	Amount	nt (A) or (D) Price		Price	Following Reported Transaction(s) (Instr. 3 and 4)		3 and	(I) (Instr. 4)		Beneficial Ownership (Instr. 4)
Common Stock					06/06/2	019		F		3,3	360(1)	D	\$38.31		179,698(2)			D	
				Table I			rities Acq , warrants					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	Derivative Security 2. Conversion or Exercise Price of Derivative 2. (Month/Day/Year) 3. Transaction Date (Inst. (Inst						of Derivative cquired (A) or f (D) (Instr. 3,	6. Date Expirati	ion Dat			I Amount of Se Security (Instr	curities Underlyi 3 and 4)	Der	Price of rivative curity (Instr.	9. Numb derivativ Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Code	v	(A) (D)				Expiration Nu		Amount or Number of Shares			Owned Following Reported Transaction (Instr. 4)							

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 618 shares acquired on May 15, 2019 through the Issuer's Employee Stock Purchase Plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/07/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	. Name and Address of Reporting Person* Yu K Peony							ing Symbol				(Check	ionship of Reporting F all applicable) Director	. ,	10% O		
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		06/12/201	Earliest Trar	isaction (Mo	ontn/Day/Ye	ear)				X		,	Other (lical Officer	specify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	e of Original	Filed (Mor	ith/Day	/Year)			6. Indiv	idual or Joint/Group l Form filed by O	٠, ٠	,,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by M	ore than Oi	ne Reporting Persor	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	vative Se	curities A	cquired	, Disp	osed of	f, or Ben	eficially O	wned				
1. Title of Security (Instr. 3)									Transaction 4. Securities A (Instr. 3, 4 and			ies Acquired (A) or Disposed Of I and 5)		5. Amount of Securi Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
					(MOHUI/Day/		h/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Insti		(i) (iiisti. 4)	Ownership (Instr. 4)
Common Stock					06/12/2019		M		10	10,698 A		\$14.575	190,396		D		
Common Stock					06/14/20)19		S ⁽¹⁾		3,	,420	D	\$40.96	186,976		D	
				Table I		tive Secu outs, calls						icially Owr	ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A)	or Expirat	ion Dat			d Amount of S Security (Inst	ecurities Underly : 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficia	e Form: Direct s (D) or Indirect	Indirect	
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Followin Reported Transacti (Instr. 4)	ıĭ	
Stock Option (Right to Buy)	\$14.575	06/12/2019		M			10,698	(2)		03/19/2024	Com	mon Stock	10,698	\$0.00	657	, D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

06/14/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{**} Signature of Reporting Person

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

I. Name and Address of Reporting Person* Yu K Peony						Name and Tio	cker or Tradir	g Symbol					nship of Rep I applicable Director	e)	erson(s) to	o Issuer	10% Own	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		nsaction (Mor	ith/Day/Ye	ear)				X	Officer ((give title l	below) hief Med	dical Of	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Mon	ith/Day/	/Year)			6. Individ		ed by One	e Reporti	ng Perso	on ,	
(Street) SAN FRANCISCO	CA	94	158											Form file	led by Mor	re than O	ne Repo	orting Person	
(City)	(State)	(Z	ip)																
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	, Disp	osed of	, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					Date Execution Date, if any		3. Transact Code (Inst		4. Securi (Instr. 3,		d (A) or Dispos	` ′	5. Amount o Beneficially	Owned		Direct (D	rship Form: 0) or Indirect	7. Nature of Indirect	
							Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)			and (I) (Instr. 4)		Beneficial Ownership (Instr. 4)	
Common Stock					09/06/2019			F 8,3		317(1)	D	\$41.68	178,659		D		D		
				Table I			rities Acq , warrants					cially Own es)	ed						
1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of Derivative Price of Derivat						Securities A	mber of Derivative rities Acquired (A) or osed of (D) (Instr. 3,		Exercis ion Date Day/Yea			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	8. Price of Derivative Security (Insti		9. Numb derivativ Securitie Benefici	e I	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
Security Code						(A) (D)				Expiration Num		Amount or Number of Shares	Fo Re Tr		Owned Following Reported Transaction(s) (Instr. 4)		+ ,		

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

09/10/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ting Person [*]				2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]									all ap	p of Reporting Poplicable) Director	erson(s)	to Issuer	10% Owr	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		ansaction (Mo	nth/Day/Y	ear)				X	(Officer (give title	,	edical O	` '	ecify below)				
409 ILLINOIS ST.					4. If Ame	ndment, Da	te of Original	Filed (Mo	nth/Day	/Year)			6. Indivi		or Joint/Group F Form filed by On	• .		•					
(Street) SAN FRANCISCO	CA		158												Form filed by Mo	re than (One Rep	orting Person					
(City)	(State)	(Z		Table I -	Non-Der	on-Derivative Securities Acquired, Disposed of, or Beneficially Owned						vned	<u> </u> d										
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exe	cution Date,	3. Transac Code (Ins		4. Secur (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial				
					(MONth/Day		Ab/Dau/Vaan	Code	v	Amount		(A) or (D)	Price		isaction(s) (Instr.	3 and	(i) (insti		Ownership (Instr. 4)				
Common Stock					09/16/2	.019		S		3,	419(1)	D	\$40.92		175,240			D					
				Table I		Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed											
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	ion Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) S. Date Exercisable and Expiration Date (Month/Day/Year) Expiration Date (Month/Day/Year) Title and Amount of Securities Derivative Security (Instr. 3 and Expiration Date (Month/Day/Year)									8. Price of Derivative Security (Instr. 5) 9. Nun derivat Securi Securi Benefi		Derivative deriv Security (Instr. Secu 5) Bend		Derivative derivative Security (Instr. 5) Derivative derivation derivation derivation derivation derivation derivation derivation derivation derivation derivative d		ive ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	V (A) (D) Exercisable Date Title Sh										Owned Follow Report Transa (Instr. 4	ing ed ction(s)	- '					

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/18/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person [*]						d Ticker or Trad	0 ,						onship of Reporting F Ill applicable) Director	Person(s) to		Owner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 12/04/20		t Transaction (Mo	onth/Day/Yea	ar)				X	Officer (give title	,		er (specify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Original	Filed (Mont	h/Day/	Year)			6. Individ	dual or Joint/Group l Form filed by O)
(Street) SAN FRANCISCO	CA	94	158									Form filed by M	ore than On	ne Reporting Per	son		
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Der	ivative	Securities A	Acquired,	Disp	osed of	, or Bene	eficially Ow	ned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	E	ZA. Deemed Execution Date, f any	3. Transacti Code (Instr			rities Acquired (A) or Disposed , 4 and 5)		d Of (D)	5. Amount of Securities Beneficially Owned Following Reported		6. Ownership For Direct (D) or India I) (Instr. 4)	
							Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr 4)		., (Ownership (Instr.
Common Stock					12/04/2	019		М		6	557	A	\$14.575	175,897		D	
Common Stock					12/04/2	019		M		3,	500	A	\$18	179,397		D	
Common Stock					12/06/2	019		F		3,3	60(1)	D	\$47.39	176,037		D	
				Table I			ecurities Ac						d				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securit	ber of Derivative ies Acquired (A) o ed of (D) (Instr. 3	or Expiration	on Date	9		d Amount of Sec Security (Instr.		8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficial Owned	Form: Dir (D) or Inc	ect Indirect rect Beneficial
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Following Reported Transactio (Instr. 4)		(*)
Stock Option (Right to Buy)	\$14.575	12/04/2019		M			657	(2)		03/19/2024	Common Stock		657	657 \$0.00		D	
Stock Option (Right to Buy)	\$18	12/04/2019		M			3,500	(2)		11/13/2024	Com	mon Stock	3,500	\$0.00	52,500	0 D	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Fully vested.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report	ting Person [*]				2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]									all ap	p of Reporting Poplicable) Director	erson(s)	to Issuer	10% Owr	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o		insaction (Mo	nth/Day/Ye	ear)				X	(Officer (give title	,	edical O	` '	ecify below)				
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mor	nth/Day	/Year)			6. Indiv		or Joint/Group F Form filed by On			,					
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158												Form filed by Mo	re than (One Rep	orting Person					
	<u> </u>	<u> </u>		Table I -	Non-Der	ivative Se	curities A	cquired	d, Disp	posed of	f, or Bene	eficially Ov	vned										
1. Title of Security (Instr. 3)					2. Transac Date	Exec	ution Date,	3. Transac Code (Ins		4. Secur (Instr. 3,		d (A) or Dispo	sed Of (D)	Ben	mount of Securiti	es	Direct (ership Form: (D) or Indirect	7. Nature of Indirect				
					(Month/Day		y ith/Day/Year)	Code	v	Amount		(A) or (D)	Price		owing Reported saction(s) (Instr.	3 and	(I) (Insti	r. 4)	Beneficial Ownership (Instr. 4)				
Common Stock					12/16/2	019		S		3,	420(1)	D	\$46.68		172,617			D					
				Table I		Derivative Securities Acquired, Disposed of, or Beneficially Owne (e.g., puts, calls, warrants, options, convertible securities)						ed											
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	ion Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securitie Derivative Security (Instr. 3 and									Derivative Security (Instr. 5) Geru		Derivative deri Security (Instr. Secu 5) Ben		Derivative Security (Instr. 5) derivative Security (Instr. Benerative		ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	V (A) (D) Exercisable Expiration Date Title Sh										Owned Following Reporte Transac (Instr. 4	ing ed ction(s)		* ')				

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/17/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person*				FIBRO	GEN I	d Ticker or Trad							eck all ap	ip of Reporting Poplicable) Director	erson(s) to	Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/06/20		Transaction (Mo	onth/Day/Yea	ar)					X	Officer (give title	below)	lical O	` '	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Original	Filed (Mont	h/Day/	Year)			6. li		or Joint/Group F Form filed by On			,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than Or	ne Repo	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Deri	ivative	Securities A	cquired,	Disp	osed of	, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)								Transaction 4. Securition (Instr. 3, 4)			es Acquired (A) or Disposed Of and 5)		Ben	5. Amount of Securities Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial	
					(Month/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		(1) (111011	,	Ownership (Instr. 4)
Common Stock					03/06/2	020		F		9,8	26(1)	D	\$39.71		162,791			D	
Common Stock					03/16/20	020		M		3,	750	A	\$19.39)	166,541			D	
Common Stock					03/17/2	020		A		45,0	000(2)	A	\$0.00		211,541			D	
				Table I			ecurities Ac alls, warrant			,		•	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	4. Transa (Instr. 8)	Secu		per of Derivative es Acquired (A) o ed of (D) (Instr. 3	r Expiration	on Date			I Amount of Se Security (Instr.		derlying	Derivative deri Security (Instr. Sec 5) Ben		e s	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.		
	Security			Code	v	(A)	(D)	Date Exercisa	ıble [Expiration Date	Title		Amount Number Shares			Owned Following Reported Transacti (Instr. 4)	ĭ		+ ,
Stock Option (Right to Buy)	\$19.39	03/16/2020		M			3,750	(3)		02/22/2026	Com	mon Stock	3,	750	\$0.00	56,25	50	D	
Stock Option (Right to Buy)	\$26.41	03/17/2020		A		75,00	0	(4)		03/17/2030	Comi	mon Stock	75,	,000	\$0.00	75,00	00	D	

Explanation of Responses

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Represents the grant of restricted stock units. Twenty-five percent of the restricted stock units vest on March 6, 2021, and the remainder vests in equal amounts quarterly thereafter for the following three years.
- 3 Fully vested
- 4. Twenty-five percent of the shares subject to the option vests on March 1, 2021, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/18/2020

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony		1	Name and Tion		ig Symbol	I				onship of Reporting Person(s) all applicable) Director		erson(s) to	o Issuer	10% Owr	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o	f Earliest Trai 20	nsaction (Mor	nth/Day/Ye	ear)				X	Officer	r (give title C	below) hief Med	dical Of	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Mon	nth/Day/	/Year)			6. Individ	Form f	nt/Group Fi filed by One	e Reporti	ng Perso	on	
(Street) SAN FRANCISCO	CA	94	158											Form f	filed by Mo	re than O	ne Repo	orting Person	
(City)	(State)	(Z	ip)																
			Т	able I - I	Non-Der	ivative Se	curities A	cquired	, Disp	osed of	, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transac Date	Exec	ution Date,	3. Transac Code (Inst		4. Securi (Instr. 3,		d (A) or Dispos	` '	Beneficiall	t of Securition		Direct (D	rship Form: 0) or Indirect	7. Nature of Indirect
					(Month/Day		h/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Following Reporte Transaction(s) (Inst			(I) (Instr.	4)	Beneficial Ownership (Instr. 4)
Common Stock					06/08/2	020		F		3,2	292(1)	D	\$33.61	2	208,927(2)			D	
				Table I		ative Secu puts, calls						cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative cquired (A) or f (D) (Instr. 3,	6. Date Expirat (Month/	ion Dat			Amount of Se Security (Instr.	curities Underlyii 3 and 4)	Deriv	vative urity (Instr.	9. Numb derivativ Securitie Beneficia	re I	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	V (A) (D) Date Expiration Date Title								Amount or Number of		Owned Following Reported Transaction(s) (Instr. 4)	d tion(s)		4)	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 678 shares acquired on May 15, 2020 through the Issuer's Employee Stock Purchase Plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/10/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony		1		cker or Tradi C [FGEN]	il				nship of Re Il applicable Director	le)	erson(s) to	o Issuer	10% Own	er					
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 07/24/20		nsaction (Mo	nth/Day/Ye	ear)				X	Officer	(give title	below) hief Med	dical Of	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mor	nth/Day/	Year)			6. Individ		nt/Group Fil			cable Line) on	
	CA (State)	94 (Zij	158 P)									Form fil	iled by Mor	re than O	one Repo	orting Person			
			Т	able I - I	- Non-Derivative Securities A			cquired	l, Disp	osed of	, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transaction 2A. Deemed Execution Date, (Month/Day/Year) if any			3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Beneficially	ly Owned		Direct (D	rship Form: 0) or Indirect	7. Nature of Indirect
					(Month/Day		y th/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following I Transaction 4)			(I) (Instr.	4)	Beneficial Ownership (Instr. 4)
Common Stock					07/24/2	020		S		3,3	351 ⁽¹⁾	D	\$42.35	2	205,576			D	
				Table I			rities Acc s, warrant		•			cially Own es)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	on Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 6. Date Exercisable and Expiration Date (Month/Day/Year)									8. Price of Derivative Security (Instr. 5) 9. Numb derivativ Securiti Benefic		ve i	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	V (A) (D) Exercisable Date Expiration Nu Sh										Owned Followin Reported Transact (Instr. 4)	d tion(s)		+)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

07/28/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]				FIBRO	lame and Tio	[FGEN]	>				(Check	tionship of Reporting all applicable) Director	, ,		10% Own	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		09/03/202	Earliest Trar	isaction (Mo	ontn/Day/Ye	ar)				X		,	dical Officer	٠.	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	of Original	Filed (Mon	th/Day	/Year)			6. Indiv	idual or Joint/Group Form filed by 0	٠,		e Line)	
(Street) SAN FRANCISCO	CA	94	158											Form filed by N	lore than O	ne Reporting	Person	
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative Sec	curities A	cquired	, Disp	posed of	f, or Bene	eficially Ov	vned					
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day)	Execu			3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Dispose (Instr. 3, 4 and 5)		sed Of (D)	5. Amount of Secur Beneficially Owned Following Reporte		6. Ownership Direct (D) or (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(MOHUI/Day/		h/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Inst		(1) (111511. 4)		Ownership (Instr. 4)
Common Stock					09/03/20)20		M		10),000	A	\$18	215,576		D		
Common Stock					09/03/20)20		S		10,	000(1)	D	\$50.89	205,576		D		
				Table I		tive Secu outs, calls						cially Own ies)	ied					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A)	or Expirati	ion Dat			I Amount of Se Security (Instr	ecurities Underl . 3 and 4)	8. Price of Derivative Security (Inst	9. Numb derivativ Securitie Beneficia Owned	re Form es (D) o	wnership : Direct r Indirect str. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Followin Reported Transact (Instr. 4)	d tion(s)		
Stock Option (Right to Buy)	\$18	09/03/2020		M			10,000	(2)		11/13/2024	Com	mon Stock	10,000	\$0.00	42,50	00	D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/04/2020

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

l	OMB APPROVAL	
l	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	ting Person [*]		1	Name and Tio	cker or Tradir	g Symbol					nship of Report applicable) Director	ng Person(s) to Issue	10% Owr	ner			
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o		nsaction (Mor	ith/Day/Ye	ear)				X	Officer (give		v) Medical C	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Mon	ith/Day/	/Year)			6. Individ	ual or Joint/Gro Form filed b	y One Rep	orting Per	son	
(Street) SAN FRANCISCO	CA	94	158											Form filed b	y More tha	n One Re _l	porting Person	
(City)	(State)	(Zi	p)															
			Т	able I - I	Non-Der	ivative Se	curities A	quired,	, Disp	osed of	, or Bene	ficially Ov	ned					
1. Title of Security (Instr. 3)					2. Transac	Exec	ution Date,	3. Transact Code (Inst		4. Securi (Instr. 3,		d (A) or Dispos	` ′	5. Amount of Se Beneficially Ow	ned	Direct	ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		h/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Following Repo Transaction(s) (4)		(I) (Ins	tr. 4)	Ownership (Instr. 4)
Common Stock					09/08/2	020		F		3,2	291(1)	D	\$42.16	202,2	85		D	
				Table I			rities Acq , warrants					cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative cquired (A) or f (D) (Instr. 3,	6. Date Expirati (Month/l	ion Dat			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	8. Price of Derivative Security (I 5)	deriv Secu Bene	rities eficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	Date Expiration No							Amount or Number of Shares		Repo	owing orted saction(s)		-*/	

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

09/10/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
١	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	1. Name and Address of Reporting Person* Yu K Peony							g Symbol					5. Relation (Check a	II app	o of Reporting Pe blicable) birector	erson(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/16/20	f Earliest Trar 20	nsaction (Mon	th/Day/Yea	ar)				X	C	Officer (give title	,	edical O	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Month	h/Day/	Year)			6. Individ		r Joint/Group Fi form filed by On			,	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158											F	orm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(21		able I - I	Non-Deri	vative Sec	curities A	quired,	Disp	osed of	, or Bene	ficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu	ition Date,	3. Transaction		4. Securi (Instr. 3,		d (A) or Dispos	sed Of (D)	Bene	mount of Securiti eficially Owned owing Reported	ies		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Day		h/Dau/Vaan	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (iiisti	4)	Ownership (Instr. 4)
Common Stock					09/16/2	020		S		3,3	351 ⁽¹⁾	D	\$44.01		198,934			D	
				Table I		ntive Secu puts, calls			•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities Ad Disposed of 4 and 5)	cquired (A) or	6. Date E Expiratio (Month/D	n Date	е		Amount of Se Security (Instr	curities Underlyi 3 and 4)	ng	8. Price of Derivative Security (Instr. 5)	9. Numl derivati Securiti Benefic	ive ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	Date Expiration No							Amount or Number of Shares	er of		Owned Followin Reported Transacti (Instr. 4)	ed owing orted saction(s)		- ',

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

09/18/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	1. Name and Address of Reporting Person* Yu K Peony							g Symbol						nship of Reporting I applicable) Director	Person(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/07/20	f Earliest Trar 20	nsaction (Mon	th/Day/Yea	ar)				X	Officer (give titl	e below) Chief Me	edical Ot		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Mont	th/Day/	Year)			6. Individ	ual or Joint/Group Form filed by C			,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by N	ore than (One Repo	orting Person	
(City)	(State)	(Zi																
			Т	able I - I	Non-Deri	vative Sec	curities A	quired,	Disp	osed of	, or Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu	ition Date,	3. Transact Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	` '	5. Amount of Secur Beneficially Owned Following Reporte			ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Day		h/Day/Voor)	Code	v	Amount		(A) or (D)		Transaction(s) (Inst 4)		(i) (ilisti	. 4)	Ownership (Instr. 4)
Common Stock					12/07/2	020		F		3,2	292(1)	D	\$41.99	195,642			D	
				Table I		itive Secu outs, calls	•	-	•			cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number o Securities A Disposed of 4 and 5)	cquired (A) or	6. Date E Expiration (Month/E	on Date			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	8. Price of Derivative Security (Instr 5)	9. Num derivati Securiti Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

12/09/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
١	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Yu K Peony	I. Name and Address of Reporting Person* Yu K Peony							g Symbol					5. Relation (Check a	II ap	p of Reporting Pe plicable) Director	erson(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/16/20	f Earliest Trar 20	nsaction (Mon	th/Day/Year)				X	(Officer (give title	,	edical O	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Month	/Day/\	Year)			6. Individ		or Joint/Group Form filed by On	• .		,	
	CA (State)	94 (Zi	158											F	Form filed by Mo	ore than (One Rep	orting Person	
(City)	(State)	(Σι		able I - I	 Non-Deri	vative Sec	curities Ac	quired, [Disp	osed of	, or Bene	ficially Ov	/ned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu	ition Date,	3. Transactio Code (Instr.		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	ies		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(WOIIII/Day		h/Dau/Vaan	Code V	,	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (iiisti	4)	Ownership (Instr. 4)
Common Stock					12/16/2	020		S		3,3	350 ⁽¹⁾	D	\$41.61		192,292			D	
				Table I		itive Secu outs, calls			•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number o Securities Ad Disposed of 4 and 5)	cquired (A) or	6. Date Ex Expiration (Month/Da	n Date			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	ng	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securiti Benefic Owned	ive ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisab		expiration Pate	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ing ed ction(s)		- ',

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/17/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

EXHIBIT BBB

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Conterno Enrique A	ting Person [*]		FIBRO	GEN IN	icker or Trad]				(Chec	k all ap	ip of Reporting Pe plicable) Director	erson(s) t	to Issuer	10% Own	er					
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/10/20		ansaction (Mo	onth/Day	y/Year)				2	X (Officer (give title	below) nief Exec	cutive C	` '	ecify below)		
409 ILLINOIS STREET					4. If Ame	ndment, Da	te of Original	Filed (I	Month/Day	//Year)					or Joint/Group F Form filed by On						
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	re than C	One Rep	orting Person			
(City)	(State)	(Zi	p)																		
			Т	able I -	Non-Deri	vative S	ecurities A	cquir	ed, Dis	posed of	f, or Ben	eficially O	vned								
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exe	Deemed cution Date,	3. Tran Code (saction Instr. 8)	4. Securi (Instr. 3,	ities Acquire 4 and 5)	sed Of (D)	Ben	5. Amount of Securities Beneficially Owned Following Reported			ership Form: D) or Indirect	7. Nature of Indirect Beneficial			
					(MOIIII/Day		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		(i) (ilisti	. 4)	Ownership (Instr. 4)		
Common Stock					06/10/2	020		P		8	,000	A	\$36.2853 ⁽¹⁾		8,000			I	By Trust		
Common Stock					06/11/20)20		P		19	9,800	A	\$35.2828(2)		27,800			I	By Trust		
Common Stock															60,000			D			
				Table I			urities Ac s, warrant	•		,		icially Owr	ed								
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	of Derivative Acquired (A) o of (D) (Instr. 3	r Exp	Date Exerci Diration Da Onth/Day/Ye	te		d Amount of S Security (Inst	ecurities Under . 3 and 4)	rlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	ve ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.		
	Security			Code	v	V (A) (D) Exercisable Expiration N Title Si											Folio Repo		ng ed ction(s)		-,

Explanation of Responses:

- 1. The shares were purchased in the open market at prices ranging from \$35.75 to \$36.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares purchased at each separate price.
- 2. The shares were purchased in the open market at prices ranging from \$35.22 to \$35.42. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares purchased at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/12/2020

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Reporting Person* Conterno Enrique A					2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]									II applio	of Reporting Pe cable) ector	erson(s) t	to Issuer	10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of Earliest Transaction (Month/Day/Year) 01/06/2021 4. If Amendment, Date of Original Filed (Month/Day/Year)									Officer (give title below)			Other (specify below) ecutive Officer		
409 ILLINOIS STREET														6. Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person					
(Street) SAN FRANCISCO	CA	94	158											For	rm filed by Mo	re than C	One Rep	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Der	ivative S	ecurities A	Acqui	ired, Dis	posed o	f, or Bene	ficially Ov	vned						
1. Title of Security (Instr. 3)				2. Transac Date (Month/Day	Exe	2A. Deemed Execution Date, if any (Month/Day/Year)				ities Acquire 4 and 5)	` '	Benefi	Amount of Securities		6. Ownership Form: Direct (D) or Indirect		7. Nature of Indirect Beneficial		
				(Month/Day				· v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)		(I) (Instr. 4)		Ownership (Instr. 4)		
Common Stock			01/06/2021			F		5,4	411(1)	D	\$38.31	55,273(2)		D			
Common Stock															27,800			I	By Trust
				Table I			urities Ac ls, warrant	•		-		-	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	onversion r Exercise (Month/Day/Year) rice of erivative	Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	mber of Derivative rities Acquired (A) or osed of (D) (Instr. 3, 5)		Date Exerc opiration Da lonth/Day/Yo	ite	Derivative Security			8. Price of Derivative Security (Ins 5)		9. Numb derivati Securiti Benefic Owned	ive Form: Directies (D) or Indirectially (I) (Instr. 4)		11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	V (A)		(D)	Dat Exe	ate cercisable	Expiration Date	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4)	ed tion(s)	(s)	,

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 684 shares acquired on November 13, 2020 through the Issuer's Employee Stock Purchase Plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

01/08/2021

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

** Signature of Reporting Person

Date

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Conterno Enrique A	ting Person [*]				FIBRO	GEN IN	cker or Tradii						5. Relatio (Check a		,	erson(s) t	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		07/06/20		nsaction (Mo	nth/Day/Y	ear)				X	Offic	cer (give title Ch	,	cutive O	` '	ecify below)
409 ILLINOIS STREET					4. If Ame	ndment, Dat	e of Original	Filed (Mo	nth/Day	/Year)			6. Individ		oint/Group Fi m filed by One				
(Street) SAN FRANCISCO	CA	94	158											Form	m filed by Mo	re than (One Repo	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Deri	vative Se	curities A	cquirec	d, Disp	posed of	, or Bene	ficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	ution Date,	3. Transa Code (Ins		4. Securi		d (A) or Dispo		Benefici	unt of Securition in the securition in the security of the sec	es		rship Form: 0) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		th/Day/Year)	Code	v	Amount		(A) or (D)	Price		tion(s) (Instr.	3 and	(I) (INST.	4)	Ownership (Instr. 4)
Common Stock					07/06/2	021		F		1,8	359 ⁽¹⁾	D	\$25.06		136,098(2)			D	
Common Stock															27,800			I	By Trust
				Table I			rities Acq s, warrants					cially Own	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative acquired (A) of f (D) (Instr. 3,	Expira	e Exerci ation Dat n/Day/Ye			Amount of Se Security (Instr	curities Underlyi	Dei	Price of erivative ecurity (Instr.	9. Numb derivativ Securiti Benefic Owned	ve ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4)	ng ed etion(s)		,

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 684 shares acquired on May 14, 2021 through the Issuer's Employee Stock Purchase Plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/08/2021

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

** Signature of Reporting Person

Date

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

EXHIBIT CCC

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Check this box if no longer subject to Section 16. For	m
4 or Form 5 obligations may continue. See Instruction	1
1(b).	

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden
hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]				FIBRO	OGEN IN	cker or Tradir						5. Relation (Check a	ıll apı	p of Reporting Po plicable) Director	erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		nsaction (Mor	nth/Day/Ye	ar)				X	C	Officer (give title		nce and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	endment, Dat	e of Original	Filed (Mont	th/Day/	/Year)			6. Individ		or Joint/Group F Form filed by On	•		•	
(Street) SAN FRANCISCO	CA	94	158											F	Form filed by Mo	ore than (One Rep	orting Person	
(City)	(State)	(Zi		Tabla I	Nan Dar	ivetive Ce	i4i A	id	Diam		D	eficially Ov							
1. Title of Security (Instr. 3)			<u>'</u>	able I -	2. Transac			3. Transact	•	1		eficially Ov		5. Aı	mount of Securiti	ies		ership Form:	7. Nature of
					Date (Month/Day	y/Year) if an	y 4h/Dau/Yaan)	Code (Insti	r. 8) V	(Instr. 3,	4 and 5)	(A) or (D)	Price	Follo	eficially Owned owing Reported saction(s) (Instr.	3 and	Direct (D) or Indirect r. 4)	Indirect Beneficial Ownership (Instr. 4)
Common Stock					06/01/2	016		F		1,9	958(1)	D	\$18.89		139,910			D	
				Table I			ırities Acq s, warrants		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) or f (D) (Instr. 3,		on Dat			I Amount of Se Security (Instr	curities Underly 3 and 4)	ng	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securiti Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

06/03/2016

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

Check this box if no longer subject to Section 16. Form

4 or Form 5 obligations may continue. See Instruction

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEM

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ng Person [*]					Name and Tio		g Symbol						onship of Reporting II applicable) Director	Person(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/15/20	f Earliest Trar 16	nsaction (Mor	th/Day/Yea	ar)				X	Officer (give ti	e below) VP, Fina	nce and	Other (spe	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Monti	h/Day/`	Year)			6. Individ	lual or Joint/Group Form filed by 0	٠.	• • •	,	
	CA (State)	94 (Zi	158 P)											Form filed by I	fore than (One Repo	orting Person	
			Т	able I - I	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	, or Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact	Execu	ution Date,	3. Transacti Code (Instr.		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Secu Beneficially Owner		Direct (E	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		h/Day/Voor)	Code	v	Amount		(A) or (D)	Price	Following Reporte Transaction(s) (Ins 4)		(I) (Instr.	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					06/15/2	016		S		1,7	796 ⁽¹⁾	D	\$16.49	138,114			D	
				Table I		ntive Secu puts, calls			•			cially Own es)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) or (D) (Instr. 3,	6. Date E Expiration (Month/D	on Date	•		Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Inst	Benefic	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Owned Following Reported Transact (Instr. 4	ing ed ction(s)		4)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Melissa Navarro, Attorney-in-fact

06/16/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Repor Cotroneo Pat	ting Person [*]				FIBRO	GEN IN	cker or Tradi C [FGEN]						5. Relation (Check a	II app	o of Reporting Pe blicable) birector	erson(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 09/01/20		insaction (Mo	nth/Day/Y	'ear)				X	C	Officer (give title		nce and		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	e of Original	Filed (Mo	onth/Day	/Year)			6. Individ		r Joint/Group Fi orm filed by On				
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158											F	orm filed by Mo	re than (One Rep	orting Person	
(Oily)	(Olulo)	(2)		able I - I	Non-Deri	ivative Se	curities A	cquired	d, Disp	posed of	, or Bene	ficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec		3. Transac Code (Ins		4. Securi		d (A) or Dispo	sed Of (D)	Bene	mount of Securiti eficially Owned owing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Da)		th/Day/Year)	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (iiisti	4)	Ownership (Instr. 4)
Common Stock					09/01/2	016		F		1,4	410 ⁽¹⁾	D	\$17.33		136,704			D	
				Table I			urities Acc s, warrant					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	of Derivative Acquired (A) o f (D) (Instr. 3,	r Expira	e Exercis ation Dat h/Day/Yea			Amount of Se Security (Instr	curities Underlyi 3 and 4)	ng	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securiti Benefic Owned	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ing ed ction(s)		- ',

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

09/02/2016

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Reporticular Cotroneo Pat	ng Person [*]					Name and Tio		g Symbol						onship of Reporting Il applicable) Director	Person(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/12/20	f Earliest Trar 16	nsaction (Mor	ith/Day/Yea	ar)				X	Officer (give tit	e below) VP, Fina	nce and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Monti	h/Day/`	Year)			6. Individ	lual or Joint/Group Form filed by C	٠.		•	
	CA (State)	94 (Zi	158 p)											Form filed by M	ore than (One Repo	orting Person	
			Т	able I - I	Non-Deri	vative Se	curities A	quired,	Disp	osed of	, or Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact	Execu	ution Date,	3. Transacti Code (Instr.		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Secur Beneficially Owned		Direct (E	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		h/Day/Voor)	Code	v	Amount		(A) or (D)	Price	Following Reporte Transaction(s) (Inst 4)		(I) (Instr.	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					09/12/2	016		S		2,3	345(1)	D	\$18.22	134,359			D	
				Table I		itive Secu puts, calls			•			cially Own es)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		f Derivative cquired (A) or (D) (Instr. 3,	6. Date E Expiration (Month/D	on Date	•		Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr	Benefic	ve ies	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Owned Followi Reporte Transac (Instr. 4	ed ction(s)		4)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/14/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person*						cker or Tradir	ig Symbol					5. Relatio (Check a	ll appli	of Reporting Pe cable)	erson(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 12/01/20		nsaction (Mor	nth/Day/Yea	ar)				X		ficer (give title	,	nce and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mont	th/Day/	Year)			6. Individ		Joint/Group Fi rm filed by On	• •		,	
(Street) SAN FRANCISCO	CA	94	158											For	rm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi																	
			Т	able I - I	Non-Deri	ivative Se	curities A	cquired,	, Disp	osed of	, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transaci Date	Exec	ution Date,	3. Transact Code (Instr		4. Securi		d (A) or Dispo	sed Of (D)	Benefi	ount of Securiti	es	Direct (I	rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		Ab/Dau/Vaan	Code	v	Amount		(A) or (D)	Price		ving Reported action(s) (Instr.	3 and	(I) (Instr	. 4)	Ownership (Instr. 4)
Common Stock					12/01/2	016		F		1,4	410 ⁽¹⁾	D	\$20.55		134,592			D	
				Table I			ırities Acq s, warrants		•	-		cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative Acquired (A) or f (D) (Instr. 3,	6. Date I Expiration (Month/I	on Date			Amount of Se Security (Instr	curities Underlyi 3 and 4)	Ĭ D		9. Numi derivati Securiti Benefic Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ed tion(s)		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

12/02/2016 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Cotroneo Pat	ting Person [*]				FIBRO	OGEN IN	icker or Tradi C [FGEN]						5. Relation (Check a	all ap	p of Reporting Poplicable) Director	erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o		ansaction (Mo	nth/Day/Y	Year)				X	(Officer (give title	,	ince and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	te of Original	Filed (Mo	onth/Day	/Year)			6. Individ		or Joint/Group F Form filed by On			•	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158											F	Form filed by Mo	ore than	One Rep	orting Person	
				Table I -	Non-Der	ivative S	curities A	cquire	d, Dis _l	posed of	f, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exe		3. Transa Code (Ins		4. Secur (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	ies		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MONth/Day		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (insti	r. 4)	Ownership (Instr. 4)
Common Stock					12/12/2	.016		S		2,	344 ⁽¹⁾	D	\$22.05		132,248			D	
				Table I			urities Acc s, warrant	•	•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) of of (D) (Instr. 3,	r Expira	te Exerci ation Da h/Day/Ye			d Amount of Se Security (Instr	curities Underly . 3 and 4)	ing	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securit Benefic	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerc		Expiration Date	Title		Amount or Number of Shares			Owned Following Reported Transact (Instr. 4	ing ed ction(s)		* ')

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/14/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trad		I					onship of Reporting F all applicable) Director	Person(s) to	Issuer	ier
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 01/11/20		Fransaction (Mo	onth/Day/Ye	ear)				X	Officer (give title	,		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, C	ate of Original	Filed (Mor	nth/Day/	/Year)			6. Indivi	dual or Joint/Group F Form filed by Or	٠.	, ,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than On	ne Reporting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	ivative S	Securities A	cquired	l, Disp	osed of	, or Bene	eficially Ov	wned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	A. Deemed recution Date, any	3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispo	sed Of (D)	5. Amount of Securit Beneficially Owned Following Reported	0	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
					(MOIIII/Day		lonth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr.		i) (iiisti. 4)	Ownership (Instr. 4)
Common Stock					01/11/2	017		M		6	,500	A	\$2.35	138,748		D	
Common Stock					01/11/2	017		S		6,5	500(1)	D	\$24	132,248		D	
				Table I			curities Ac Ills, warrant						ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative s Acquired (A) o d of (D) (Instr. 3	r Expirat	Exercistion Date Day/Yea			d Amount of So Security (Instr	ecurities Underly : 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficial Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Following Reported Transactio (Instr. 4)	ĭ	
Stock Option (Right to Buy)	\$2.35	01/11/2017		М			6,500	(2)		03/12/2018	Com	mon Stock	6,500	\$0.00	18,500	0 D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

01/13/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{**} Signature of Reporting Person

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Rep Cotroneo Pat	orting Person*						d Ticker or Trad	0 ,						onship of Reporting P Ill applicable) Director	erson(s) to Is	ssuer 10% Owr	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/01/20		t Transaction (Mo	onth/Day/Ye	ar)				X	Officer (give title	below) VP, Finance		ecify below)	
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Original	Filed (Mont	th/Day/`	Year)		6. Individ	,					
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than One	Reporting Person		
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	ivative	Securities A	cquired,	Disp	osed of	, or Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		2A. Deemed Execution Date, if any	3. Transact Code (Insti		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Securit Beneficially Owned Following Reported	Dir	Ownership Form: rect (D) or Indirect (Instr. 4)	7. Nature of Indirect Beneficial	
					((Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr. 4)		(Ownership (Instr. 4)	
Common Stock					03/01/2	017		М		ç	900	A	\$2.35	133,148		D		
Common Stock					03/01/2017			S		9(00(1)	D	\$26	132,248		D		
Common Stock					03/02/2	017		M		5,	5,600 A		\$2.35	137,848		D		
Common Stock					03/02/2	017		S		5,€	500(1)	D	\$26	132,248	D			
				Table I			ecurities Ac						d					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	tion Code Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year)								8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficially Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr.	
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares	mount or umber of		n(s)	7)	
Stock Option (Right to Buy)	\$2.35	03/01/2017		M			900	(2)	0	03/12/2018	Comr	mon Stock	900	\$0.00		D		
Stock Option (Right to Buy)	\$2.35	03/02/2017		M			5,600	(2)	0	03/12/2018	Comr	mon Stock	5,600 \$0.00 12,000 D					

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini. Attorney-in-fact

03/03/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trad		ol					ck all ap	nip of Reporting Poplicable)	erson(s) to	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/06/20		ransaction (M	onth/Day/Y	ear)						Officer (give title	,	ice and CFO	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amei	ndment, Da	ate of Origina	l Filed (Mo	nth/Day	/Year)					or Joint/Group F Form filed by On	٠.	• • •	le Line)	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than Oi	ne Reportin	g Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative S	ecurities A	Acquired	d, Dis _l	posed of	f, or Ben	eficially O	wned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exe	Deemed ecution Date,	3. Transac Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ben	Amount of Securiti neficially Owned lowing Reported	·	6. Ownershi Direct (D) or (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(MONth/Day		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		(i) (instr. 4)		Ownership (Instr. 4)
Common Stock					03/06/20	017		F		4,7	727(1)	D	\$25.35		127,521		D)	
Common Stock					03/08/20	017		A		38,	235(2)	A	\$0.00		165,756		D		
				Table I			urities Ac Is, warran					icially Owr ties)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	r of Derivative Acquired (A) of (D) (Instr. 3	or Expira	e Exerci ition Dat n/Day/Ye			d Amount of S Security (Inst		erlying	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficia Owned	re Form	Ownership m: Direct or Indirect nstr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerci:		Expiration Date	Title		Amount or Number or Shares			Followin Reported Transacti (Instr. 4)	d tion(s)		1 *)
Stock Option (Right to Buy)	\$25.4	03/08/2017		A		65,000		(3)	03/08/2027	Com	nmon Stock	65,00	00	\$0.00	65,00	00	D	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Represents the grant of restricted stock units. Twenty-five percent of the restricted stock units vest on March 6, 2018, and the remainder vests in equal amounts quarterly thereafter for the following three years.
- 3. Twenty-five percent of the shares subject to the option vests on March 1, 2018, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/08/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]				FIBRO	OGEN IN	cker or Tradir						5. Relation (Check a	II app	o of Reporting Pe blicable) birector	erson(s)	to Issuer	r 10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o 03/10/20		nsaction (Mor	nth/Day/Yea	ar)				X	C	Officer (give title	•	nce and	` '	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mont	th/Day/	/Year)			6. Individ		r Joint/Group Form filed by On			•	
(Street) SAN FRANCISCO	CA	94	158											F	orm filed by Mo	re than (One Rep	porting Person	
(City)	(State)	(Z																	
			1	Table I -	Non-Der	ivative Se	curities A	cquired,	Disp	osed of	f, or Bene	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exec	ution Date,	3. Transact Code (Instr		4. Securi		d (A) or Dispos	ed Of (D)	Bene	mount of Securiti eficially Owned owing Reported	es		ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(MOHUI/Day		Ab/Dau/Vaan	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (iiist	1. 4)	Ownership (Instr. 4)
Common Stock					03/10/2	.017		S		7,8	851(1)	D	\$25.3		157,905			D	
				Table I			ırities Acq s, warrants		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities A	of Derivative Acquired (A) or f (D) (Instr. 3,		on Dat			I Amount of Se Security (Instr	curities Underlyi 3 and 4)	Ĭ	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securiti Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/14/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report <u>Cotroneo Pat</u>		2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]										ship of Reporting Person(s) to Issuer applicable) Director		10% Own	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 04/25/20	Earliest Tran	nsaction (Mo	nth/Day/Ye	ar)					X	Officer (give title	e below) VP, Finar	nce and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amei	4. If Amendment, Date of Original Filed (Month/Day/Year)									al or Joint/Group F Form filed by Or	• .		•	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than (One Rep	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned						wned								
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu		3. Transact Code (Inst		4. Securi (Instr. 3,		d (A) or Dispo	sed Of	`´ ı	5. Amount of Securit Beneficially Owned Following Reported			ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Day		th/Day/Year)	Code	v	Amount		(A) or (D)	Price	. 1	Fransaction(s) (Instr. 1)		(i) (iiisti	. 4)	Ownership (Instr. 4)
Common Stock					04/25/20	017		M		6	,500	A	1	\$2.35	164,405			D	
Common Stock					04/25/20	017		S		6,5	500(1)	D		\$28	157,905			D	
				Table I	II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed								
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A) o	r Expirati	on Dat			d Amount of So Security (Instr			g 8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic Owned	ve ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Nu	nount or mber of ares		Followi Reporte Transac (Instr. 4)	ng ed etion(s)		
Stock Option (Right to Buy)	\$2.35	04/25/2017		M			6,500	(2)		03/12/2018	Com	mon Stock		6,500	\$0.00	5,5	000	D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

04/27/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{**} Signature of Reporting Person

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Repo Cotroneo Pat	orting Person [*]				FIBRO	GEN IN	icker or Trad							k all ap	ip of Reporting Peoplicable) Director	erson(s) to	Issuer	wner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 05/30/20		ansaction (Mo	onth/Day/Ye	ear))	χ (Officer (give title	,	Other ce and CFO	specify below)
409 ILLINOIS ST.					4. If Amer	ndment, Da	ite of Original	Filed (Mor	ith/Day	/Year)				X I	Form filed by On	e Reportin	•	
(Street) SAN FRANCISCO	CA	94	158											I	Form filed by Mo	re than On	ne Reporting Perso	
(City)	(State)	(Zi	p)															
			т	able I -	Non-Deri	ivative S	ecurities A	cquired	, Disp	osed of	f, or Ben	eficially Ov	wned					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exe	Deemed cution Date,	3. Transac Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ben	amount of Securiti neficially Owned lowing Reported	0	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
					(WOIIII/Day		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		i) (ilisti. 4)	Ownership (Instr. 4)
Common Stock					05/30/20	017		M		10	0,000	A	\$2.9		169,326(1)		D	
Common Stock					06/01/20	017		F		1,9	918 ⁽²⁾	D	\$27.6		167,408		D	
				Table I			urities Ac					icially Owr ties)	ied					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	of Derivative Acquired (A) o of (D) (Instr. 3	r Expirat	ion Dat		7. Title and Derivative	d Amount of So Security (Instr	ecurities Under . 3 and 4)	rlying	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficial Owned	Form: Direct	Indirect
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Following Reported Transactio (Instr. 4)	ĭ	 *',
Stock Option (Right to Buy)	\$2.9	05/30/2017		M			10,000	(3)		06/24/2020	Com	mon Stock	10,00	0	\$0.00	4,357	7 D	

Explanation of Responses:

- 1. Includes 1,421 shares purchased through the issuer's employee stock purchase plan on May 15, 2017.
- 2. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 3. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/01/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]				1		icker or Tradi C [FGEN]	0 ,	ol					all ap	p of Reporting Poplicable) Director	erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o		ansaction (Mo	nth/Day/Y	Year)				X	(Officer (give title	,	nce and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	endment, Da	te of Original	Filed (Mo	onth/Day	//Year)			6. Indivi		or Joint/Group F Form filed by On			•	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158 p)											ı	Form filed by Mo	ore than (One Rep	orting Person	
				Γable I -	Non-Der	ivative Se	curities A	cquire	d, Dis	posed o	f, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exe		3. Transa Code (Ins		4. Secur (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	ies		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MONth/Day		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (insti	r. 4)	Ownership (Instr. 4)
Common Stock					06/06/2	2017		F		1,	151(1)	D	\$29.05		166,257			D	
				Table I			urities Acc s, warrant		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) o of (D) (Instr. 3,	r Expira	te Exerci ation Da th/Day/Ye			d Amount of Se Security (Instr	ecurities Underly . 3 and 4)	ing	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securit Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerci		Expiration Date	Title		Amount or Number of Shares			Owned Following Reported Transact (Instr. 4	ing ed ction(s)		* ')

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

06/08/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]					Name and Tion GEN INC		g Symbol						nship of Reporting applicable) Director	Person(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/12/20	f Earliest Trar 17	nsaction (Mon	th/Day/Yea	ar)				X	Officer (give tit	e below) VP, Fina	ince and		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Mont	h/Day/	Year)			6. Individ	ual or Joint/Group Form filed by C	ne Repor	ting Perso	on	
(Street) SAN FRANCISCO	CA	94	158											Form filed by M	lore than (One Repo	orting Person	
(City)	(State)	(Zi			<u> </u>													
			Т	able I - I	Non-Deri	vative Sec	curities A	quired,	Disp	osed of	, or Bene	ficially Ov	ned					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu	ition Date,	3. Transacti Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	` ′	5. Amount of Secui Beneficially Owned Following Reporte			rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(WORLII/Day		h/Day/Voor)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Inst 4)		(i) (instr	. 4)	Ownership (Instr. 4)
Common Stock					06/12/2	017		S		2,8	891 ⁽¹⁾	D	\$28.75	163,366			D	
				Table I		itive Secu outs, calls	•		•			cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number o Securities Ad Disposed of 4 and 5)	cquired (A) or	6. Date E Expiration (Month/D	on Date			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	8. Price of Derivative Security (Inst	9. Num derivati . Securit Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Owned Following Reported Transact (Instr. 4	ing ed ction(s)		- *)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/14/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trad		I					onship of Reporting F all applicable)	Person(s) to	Issuer	ier
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/19/20		Fransaction (Mo	onth/Day/Y	ear)				X	Officer (give title	,		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, C	ate of Original	Filed (Mo	nth/Day	/Year)			6. Indiv	dual or Joint/Group F Form filed by O	٠.	,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by M	ore than On	ne Reporting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	ivative S	Securities A	cquirec	l, Disp	osed of	f, or Ben	eficially O	wned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	A. Deemed recution Date, any	3. Transa Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	5. Amount of Securing Beneficially Owned Following Reported	0	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
					(Month/Day		any Ionth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr 4)		i) (ilistr. 4)	Ownership (Instr. 4)
Common Stock					06/19/2	017		M		5	,500	A	\$2.35	168,866		D	
Common Stock					06/19/2	017		S		5,5	500(1)	D	\$30	163,366		D	
				Table I			curities Ac Ills, warrant						ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative s Acquired (A) o d of (D) (Instr. 3	or Expira	Exercis tion Dat /Day/Yea			d Amount of S Security (Inst	ecurities Underly r. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficial Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerci:		Expiration Date	Title		Amount or Number of Shares		Following Reported Transactio (Instr. 4)	ĭ	4)
Stock Option (Right to Buy)	\$2.35	06/19/2017		M			5,500	(2		03/12/2018	Com	mon Stock	5,500	\$0.00	0	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/21/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

** Signature of Reporting Person

Date

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trad		il					tionship of Reporting all applicable) Director	Person(s) t		Owner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/22/20		Transaction (Mo	onth/Day/Ye	ear)				X		,		r (specify below)
409 ILLINOIS ST.					4. If Amei	ndment, [Date of Original	Filed (Mor	nth/Day	/Year)			6. Indiv	idual or Joint/Group Form filed by	٠,)
(Street) SAN FRANCISCO	CA	94	158											Form filed by	More than C	One Reporting Per	on
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	vative	Securities A	cquired	l, Disp	osed of	f, or Bene	eficially O	wned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	E	A. Deemed xecution Date, any	3. Transac Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	5. Amount of Secu Beneficially Owne Following Reporte	d	6. Ownership Forn Direct (D) or Indire (I) (Instr. 4)	
					(Month/Day		any Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Ins		(i) (instr. 4)	Ownership (Instr.
Common Stock					06/22/20	017		M		3	,000	A	\$2.9	166,366		D	
Common Stock					06/22/20	017		S		3,0	000(1)	D	\$32	163,366		D	
				Table I			curities Ac						ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative es Acquired (A) o d of (D) (Instr. 3	r Expirat	Exercis tion Dat //Day/Yea			d Amount of S Security (Inst	ecurities Underl r. 3 and 4)	8. Price of Derivative Security (Inst	9. Numb derivativ r. Securiti Benefic Owned	ve Form: Dire ies (D) or Indi ially (I) (Instr. 4	ct Indirect rect Beneficial
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Followi Reporte Transac (Instr. 4)	ing ed ction(s)	4)
Stock Option (Right to Buy)	\$2.9	06/22/2017		M			3,000	(2))	06/09/2020	Com	mon Stock	3,000	\$0.00	22,6	600 D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ John Alden, Attorney-in-fact

06/23/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

** Signature of Reporting Person

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						Ticker or Trad		I					tionship of Reporting all applicable) Director	Person(s) to	to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 07/06/20		Transaction (Me	onth/Day/Ye	ear)				X		,		pecify below)
409 ILLINOIS ST.					4. If Amei	ndment, [Date of Origina	Filed (Mor	nth/Day	/Year)			6. Indiv	·	٠.	eck Applicable Line) ing Person	
(Street) SAN FRANCISCO	CA	94	158											Form filed by I	More than C	One Reporting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	ivative	Securities A	Acquired	l, Disp	osed of	, or Bene	eficially O	wned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	E	A. Deemed xecution Date, any	3. Transac Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	5. Amount of Secu Beneficially Owne Following Reporte	i i	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
					(Month/Day		any Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Ins		(i) (instr. 4)	Ownership (Instr. 4)
Common Stock					07/06/20	017		М		4	,000	A	\$2.9	167,366		D	
Common Stock					07/06/20	017		S		4,0	000(1)	D	\$34	163,366		D	
				Table I			ecurities Ac alls, warrant						ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative es Acquired (A) o d of (D) (Instr. 3	or Expirat	Exercis tion Dat /Day/Yea			d Amount of S Security (Inst	ecurities Underl r. 3 and 4)	8. Price of Derivative Security (Inst	9. Numb derivativ r. Securitie Benefici Owned	ve Form: Direct es (D) or Indirect	Indirect
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Followin Reporte Transact (Instr. 4)	ed tion(s)	7
Stock Option (Right to Buy)	\$2.9	07/06/2017		M			4,000	(2))	06/09/2020	Com	mon Stock	4,000	\$0.00	18,6	500 D	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/07/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

** Signature of Reporting Person

Date

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						icker or Trad							nship of Reporting F Il applicable) Director	Person(s) to Is	ssuer 10% Owi	ner			
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 08/01/20		ansaction (Mo	onth/Day/Yea	ar)		X	Officer (give title		pecify below)						
409 ILLINOIS ST.					4. If Amer	4. If Amendment, Date of Original Filed (Month/Day/Year)						6. Individ	6. Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person							
(Street) SAN FRANCISCO	CA	94	158											Form filed by M	ore than One	Reporting Person				
(City)	(State)	(Zi	ip)																	
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	, or Bene	eficially Ow	ned							
1. Title of Security (Instr. 3)			2. Transacti Date	Exe	Deemed cution Date,	3. Transaction Code (Instr. 8)		4. Securities Acq (Instr. 3, 4 and 5)		d (A) or Dispos		5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)		Ownership Form: rect (D) or Indirect	7. Nature of Indirect					
					(Month/Day	/Year) if an (Moi	y nth/Day/Year)	Code V		Amount				(A) or (D)	Price	(Instr. 4)	Beneficial Ownership (Instr 4)			
Common Stock					08/01/20	017		М		7,	,300	A	\$2.9	170,666		D				
Common Stock	Common Stock				08/01/20	017		М		3	300	A	\$14.575	170,966		D				
Common Stock					08/01/20	017		S		7,6	500(1)	D	\$33.54(2)	163,366		D				
Common Stock					08/02/2017		М		11	,300	A	\$2.9	174,666		D					
Common Stock					08/02/2017			M		9,446		A	\$14.575	184,112		D				
Common Stock					08/02/2017			s 20,746 ⁽¹⁾			D	\$34.13(3)	\$34.13 ⁽³⁾ 163,366 D							
				Table I			urities Ac s, warrant					cially Owne	ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	of Derivative Acquired (A) o of (D) (Instr. 3		n Date	•		d Amount of Sec Security (Instr.	curities Underlyii 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficially Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr			
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)	n(s)	*,			
Stock Option (Right to Buy)	\$2.9	08/01/2017		М			7,300	(4)	0	06/09/2020 Com		mon Stock	7,300	\$0.00	11,300	D				
Stock Option (Right to Buy)	\$14.575	08/01/2017		M			300	(4)	0	03/19/2024	Com	mon Stock	300	\$0.00	111,700	D				
Stock Option (Right to Buy)	\$2.9	08/02/2017		M			11,300	(4)	0	06/09/2020	Com	mon Stock	11,300	\$0.00	0	D				

	Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)														
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)		Securities Acquired (A) or		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Sec Derivative Security (Instr. 3	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect	
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$14.575	08/02/2017		М			9,446	(4)	03/19/2024	Common Stock	9,446	\$0.00	102,254	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$33.45 to \$34.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$34.00 to \$34.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/03/2023

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Rep Cotroneo Pat	orting Person*						nd Ticker or Tra	-						ionship of Reporting lall applicable)	Person(s)	to Issuer		
(Last)	(First)	(M	iddle)		3. Date of 08/08/20		st Transaction (I	Month	n/Day/Year)		X	Director 10% Owne X Officer (give title below) Other (spe-						
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment,	, Date of Origir	al File	ed (Month/Da	ay/Year)		Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person						
(Street) SAN FRANCISCO	CA	94	158											Form filed by N	lore than (One Rep	orting Person	
(City)	City) (State) (Zip)																	
			Т	able I -	Non-Deri	vative	Securities	Acq	quired, Di	sposed	f, or Ben	eficially Ow	ned					
1. Title of Security (Instr. 3)					Date Execution Date, C					I. Securities Acquired (A) or Disposed Of Instr. 3, 4 and 5)			Beneficially Owned			ership Form: D) or Indirect	7. Nature of Indirect	
							if any (Month/Day/Year)		ode V	Amoun	:	(A) or (D)	Price	Following Reporter Transaction(s) (Inst 4)		(I) (Insti	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock	Common Stock					017			M		0,000	A	\$3.5	173,366			D	
Common Stock					08/08/20	017			M		35,000	A	\$14.575	258,366			D	
Common Stock					08/08/2017				S	1),989(1)	D	\$ 49.7 ⁽²⁾	247,377			D	
Common Stock					08/08/2017				S	7	78,304 ⁽¹⁾ D		\$50.69(3)	169,073		D		
Common Stock					08/08/20	017			S	5,707 ⁽¹⁾ D \$51.28 ⁽⁴⁾ 163,366								
				Table I			Securities A					icially Own	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securi	nber of Derivativ ties Acquired (A sed of (D) (Instr. 5)) or	6. Date Exer Expiration D (Month/Day/	ate		nd Amount of Se e Security (Instr.		8. Price of Derivative Security (Instr	9. Number derivative Securitie Beneficia Owned	ive ies	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Derivative Security			Code	V (A) (D)				Date Exercisable	Expiratio Date	Title		Amount or Number of Shares			ing ed ction(s) l)		4)
Stock Option (Right to Buy)	\$3.5	08/08/2017		M			10,00	0	(5)	06/07/202	l Con	nmon Stock	10,000	\$0.00	18,0	18,000 D		
Stock Option (Right to Buy)	\$14.575	08/08/2017		M			85,00	0	(5)	03/19/202	4 Con	nmon Stock	85,000	\$0.00	17,2	254	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$49.20 to \$50.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

- 3. The shares were sold at prices ranging from \$50.20 to \$51.175. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$51.20 to \$51.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/10/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Rep Cotroneo Pat	Name and Address of Reporting Person* Cotroneo Pat							ing Symbo	I					onship of Reporting all applicable) Director	Person(s) t	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/01/20		ransaction (M	onth/Day/Ye	ear)			X	X Officer (give title below) Other (specify belo VP, Finance and CFO 6. Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person					
409 ILLINOIS ST.					4. If Amer	ndment, D	ate of Origina	Filed (Mor	nth/Day	/Year)		I						
(Street)														Form filed by N	fore than C	ne Reportin	ig Person	
SAN FRANCISCO	CA	94	158															
(City)	(State)	(Zi	p)															
	able I -	Non-Deri	vative S	ecurities A	cquired	l, Dis _l	osed of	, or Bene	eficially Ow	ned								
1. Title of Security (Instr. 3)					2. Transact Date	Ex	Execution Date,		3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed O (Instr. 3, 4 and 5)			5. Amount of Secur Beneficially Owned	icially Owned		p Form: r Indirect	7. Nature of Indirect
					(Month/Day		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)		ı ''`		Beneficial Ownership (Instr. 4)
Common Stock					09/01/20	017		F		1,9	959 ⁽¹⁾	D	\$49	161,407		D)	
Common Stock					09/06/20	017		F	F		1,151(1)		\$48.1	160,256		D)	
				Table I			urities Ac Is, warrant	. ,	•	,		cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	(Instr. 3) Conversion or Exercise (Month/Day/Year) Execution Date, (Instr. if any Price of Pr							6. Date Expirat (Month	tion Da			d Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr. 5)		ve Fori	Ownership m: Direct or Indirect Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Derivative Security	Code	v	4 and 5)			Date Expiration Exercisable Date		Nu		Amount or Number of Shares		Owned Followin Reporte Transact (Instr. 4)	d tion(s)		4)		

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/06/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person*			Name and Tion (Name Inc.)		il				Relationship of Reporting Person(s) to Is (Check all applicable) Director				10% Owr	ier				
(Last) C/O FIBROGEN, INC.	(First)	(N	liddle)		3. Date o 09/11/20	f Earliest Tra 17	nsaction (Mo	nth/Day/Ye	ear)				X	Officer	er (give title V	,	nce and (ecify below)
409 ILLINOIS ST.			4. If Amendment, Date of Original Filed (Month/Day/Year)									Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person							
(Street) SAN FRANCISCO (City)	CA (State)		i-158								Form t	filed by Mo	re than C	One Repo	orting Person				
(City)	(State)	(2		able I -	Non-Der	ivative Se	curities A	cquired	l, Disp	posed of	f, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					Date Execution Date, if any (Month/Day/Year)		Execution Date,		ction tr. 8)	4. Secur (Instr. 3,		ed (A) or Dispos	sed Of (D)	5. Amount of Securit Beneficially Owned Following Reported			Direct (D	rship Form: 0) or Indirect	7. Nature of Indirect Beneficial
							Code	v	Amount	Amount (A) or (D) Price		Price	Transaction(s) (Instr. 3 and 4)			(I) (Instr. 4)		Ownership (Instr. 4)	
Common Stock					09/11/2	017		S		2,	851(1)	D	\$49.45		157,405			D	
				Table I		ative Secu puts, calls			•	-		cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of Derivative Security 3. Transaction Date (Month/Day/Year) 4. Transaction Date (Instr. 8) 6 April 1 April 2 Ap						Securities A	umber of Derivative irities Acquired (A) or osed of (D) (Instr. 3, d 5)		Exercistion Dat Day/Ye			d Amount of Se Security (Instr	curities Underly 3 and 4)	Deriv	Derivative der Security (Instr. 5) Ber		ve I	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
						(A) (D)			Date Expir		xpiration Nur		Amount or Number of Shares	Fo Ro Tr		Owned Following Reported Transaction(s) (Instr. 4)			

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/13/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Case 3:21-cv-02623-EMC Document 111 Filed 01/14/22 Page 1476 of 1730

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat			Name and Tio		g Symbol				5. Relation (Check a	l app	of Reporting Pe licable) irector	erson(s)	to Issuer	10% Owr	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/01/20	f Earliest Trar 17	nsaction (Mor	th/Day/Yea	ır)				X	0	fficer (give title	,	nce and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original I	iled (Month	n/Day/`	Year)			6. Individ		r Joint/Group Fi orm filed by On	• .		*	
	CA		158											F	orm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi		able I - I	Non-Deri	vative Sec	curities A	quired,	Disp	osed of	, or Bene	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu	ıtion Date,	3. Transaction		4. Securi (Instr. 3,		d (A) or Dispos	` ′	Bene	nount of Securiti	es	Direct (ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(WOITH/Day		h/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)		3 and	(I) (Instr. 4)		Ownership (Instr. 4)
Common Stock					12/01/2	017		F		1,9	9 58 ⁽¹⁾	D	\$47.15		187,854			D	
				Table I		itive Secu outs, calls			•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	Date Expiration Nu									9. Numb derivati Securiti Benefic Owned	urities (D) or Ind eficially (I) (Instr.		11. Nature of Indirect Beneficial Ownership (Instr.		
	Security			Code							ration Nu		Amount or Number of Shares	Fol Re Tra		Followi Reporte	owing orted isaction(s)		

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/05/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat			Name and Tio		g Symbol				5. Relatio (Check a	l appl	of Reporting Pe licable) rector	erson(s)	to Issuer	10% Own	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/06/20	f Earliest Trar 17	nsaction (Mon	th/Day/Year	-)				X	Ot	fficer (give title	,	nce and		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Month	/Day/Y	Year)			6. Individ		Joint/Group Fi	• .		•	
	CA (State)	94 (Zi	158											Fo	orm filed by Mo	re than (One Rep	orting Person	
(o.y)	(ciato)	,		able I - I	Non-Deri	vative Sec	curities Ac	quired, I	Dispo	osed of	, or Bene	ficially Ov	/ned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu	ition Date,	3. Transactio Code (Instr.		4. Securit (Instr. 3,		d (A) or Dispos	` ′	Benet	nount of Securiti ficially Owned wing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(WOIIII/Day		h/Dau/Vaan	Code V	,	Amount		(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)		3 and	(i) (iiisti	. 4)	Ownership (Instr. 4)
Common Stock					12/06/2	017		F		1,1	51(1)	D	\$44.85		186,703			D	
				Table I		itive Secu outs, calls	•		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year)									Beneficially		10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.		
	Security			Code	v	(A)	(D)	Date Exercisab		xpiration ate	ntion Nun		Amount or Number of Shares	Follo Repo Trans		Owned Followi Reporte Transac (Instr. 4	wing rted saction(s)		- ',

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

12/08/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]		FIBRO	OGEN IN	cker or Tradir					5. Relatio (Check a	ll appl	of Reporting Pe licable) irector	erson(s)	to Issuer	10% Owr	er			
(Last) C/O FIBROGEN, INC.	(First)	(N	liddle)		3. Date o 12/11/20		nsaction (Mo	nth/Day/Ye	ar)				X	Of	fficer (give title	below) /P, Fina	nce and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mon	th/Day	/Year)			6. Individ		r Joint/Group Fi orm filed by On			•	
(Street) SAN FRANCISCO	CA	94	158											Fo	orm filed by Mo	ore than (One Rep	orting Person	
(City)	(State)	(Z		Table I -	Non-Der	ivative Se	curities A	cauired.	Disr	oosed of	f. or Bene	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	tion 2A. I	Deemed oution Date,	3. Transact Code (Inst	tion	_	ities Acquire	d (A) or Dispos	ed Of (D)	Benef	nount of Securiti ficially Owned wing Reported	ies		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MONth/Day		Ab/Day/Vaan	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (instr		Ownership (Instr. 4)
Common Stock					12/11/2	017		S		2,8	851(1)	D	\$46		183,852			D	
				Table I			ırities Acq s, warrants					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	tion Code 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securities Derivative Security (Instr. 3 and Derivative Security								Ĭ	Derivative Security (Instr. 5)		ber of ve ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	Date Expiration N						Amount or Number of Shares	Folio Repo Tran		Owned Followi Reporte Transac (Instr. 4	lowing ported nsaction(s)		* ')		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/13/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Signature of Reporting Person

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]			lame and Tio		0 ,							ship of Reporting Po applicable)	erson(s) to	o Issuer	10% Own	er		
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 01/22/201	Earliest Trar	nsaction (Mo	onth/Day/Yea	ar)					X	Officer (give title	below) /P, Financ	ce and C	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amer	4. If Amendment, Date of Original Filed (Month/Day/Year)								. Individua	al or Joint/Group F Form filed by On	٠.		,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than Oi	ne Repo	rting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Sec	curities A	cquired,	Disp	osed of	, or Ben	eficially O	wned						
1. Title of Security (Instr. 3)					Date	2. Transaction Date Execution Date, Month/Day/Year) if any 2. Deemed Execution Date, Month/Day/Year) if any 2. Transaction Code (Instr. 8) 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)					В	. Amount of Securiti seneficially Owned ollowing Reported			ship Form:) or Indirect 4)	7. Nature of Indirect Beneficial			
					(monan zuy		n/Day/Year)	Code	v	Amount		(A) or (D)	Price		ransaction(s) (Instr.		(., (,	Ownership (Instr. 4)
Common Stock					01/22/20)18		M		25	5,000	A	\$1	8	208,852			D	
Common Stock					01/22/20)18		S		11,	802(1)	D	\$48.2	8(2)	197,050			D	
Common Stock					01/22/20)18		S		13,	198(1)	D	\$49.1	1(3)	183,852			D	
				Table I		tive Secu outs, calls						icially Owr ties)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	saction Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securitie Derivative Security (Instr. 3 and Month/Day/Year)								8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficia	re F	10. Ownership Form: Direct D) or Indirect I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)		
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amou Numb Share	er of		Followin Reported Transacti (Instr. 4)	ď		
Stock Option (Right to Buy)	\$18	01/22/2018		M			25,000	(4)		11/13/2024	Com	nmon Stock	2	25,000	\$0.00	31,00	00	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$47.80 to \$48.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$48.80 to \$49.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Rep Cotroneo Pat	porting Person*				Ticker or Trac		ol					ionship of Reporting P all applicable) Director	erson(s) to Iss	uer 10% Owr	ner		
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 02/15/20		ransaction (M	onth/Day/`	Year)				X	Officer (give title	below) VP, Finance a	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	l Filed (M	onth/Day	/Year)			6. Indivi	dual or Joint/Group F Form filed by On			
(Street) SAN FRANCISCO	CA	94	1158											Form filed by Mo	ore than One F	Reporting Person	
(City)	(State)	(Zi	ip)														
			Т	able I -	Non-Deri	vative \$	Securities A	Acquire	d, Dis	osed of	, or Ben	eficially O	vned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	Deemed ecution Date,	3. Transa Code (In		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	5. Amount of Securit Beneficially Owned Following Reported	Dire	wnership Form: ct (D) or Indirect nstr. 4)	7. Nature of Indirect Beneficial
					(MOIIII/Day		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr.		15(1.4)	Ownership (Instr
Common Stock					02/15/20	018		М		23	,540	A	\$18	207,392		D	
Common Stock					02/15/20	018		М		22	2,000	A	\$29.66	229,392		D	
Common Stock					02/15/20	018		S		1,9	000(1)	D	\$54.5 ⁽²⁾	227,492		D	
Common Stock					02/15/20	018		S		16,	210(1)	D	\$55.35 ⁽³⁾	211,282		D	
Common Stock					02/15/20	018		S		23,	730 ⁽¹⁾	D	\$56.29 ⁽⁴⁾	187,552		D	
Common Stock					02/15/20	018		S		3,7	700 ⁽¹⁾	D	\$56.94 ⁽⁵⁾	183,852		D	
Common Stock					02/16/20	018		М		3,	960	A	\$18	187,812		D	
Common Stock					02/16/20	018		S		3,4	100(1)	D	\$56.2 ⁽⁶⁾	184,412		D	
Common Stock					02/16/20	018		S		56	50(1)	D	\$56.76 ⁽⁷⁾	183,852		D	
				Table I			curities Ac						ed				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative s Acquired (A) l of (D) (Instr. 3	or Expir	te Exerci ation Dat th/Day/Ye			d Amount of S Security (Inst	ecurities Underly . 3 and 4)	8. Price of Derivative Security (Instr.	9. Number of derivative Securities Beneficially Owned	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr
	Security			Code	v	(A)	(D)	Date Exerc		Expiration Date	Title		Amount or Number of Shares		Following Reported Transaction(s (Instr. 4))	* /

Stock Option (Right to Buy)	\$18	02/15/2018	M		23,540	(8)	11/13/2024	Common Stock	23,540	\$0.00	7,460	D	
Stock Option (Right to Buy)	\$29.66	02/15/2018	M		22,000	(8)	03/04/2025	Common Stock	22,000	\$0.00	42,136	D	
Stock Option (Right to Buy)	\$18	02/16/2018	M		3,960	(8)	11/13/2024	Common Stock	3,960	\$0.00	3,500	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$53.85 to \$54.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$54.85 to \$55.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$55.85 to \$56.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$56.85 to \$57.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$55.60 to \$56.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$56.65 to \$57.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

02/16/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]				1		icker or Tradi	0 ,	ool				5. Relati (Check	all ap	p of Reporting Poplicable) Director	erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 03/01/20		ansaction (Mo	onth/Day/\	Year)				X	(Officer (give title	,	nce and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	endment, Da	te of Original	Filed (Mo	onth/Day	//Year)			6. Indivi		or Joint/Group F Form filed by On	•		•	
(Street) SAN FRANCISCO (City)	CA (State)	94	158											•	Form filed by Mo	re than (One Rep	orting Person	
(-13)	()	(-		Γable I -	Non-Der	ivative S	ecurities A	cquire	d, Dis	posed of	f, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exe		3. Transa Code (In		4. Secur (Instr. 3,		d (A) or Dispo	sed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MONth/Day		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		owing Reported Isaction(s) (Instr.	3 and	(i) (insti	r. 4)	Ownership (Instr. 4)
Common Stock					03/01/2	2018		F		1,	860(1)	D	\$54.95		181,992			D	
				Table I			urities Acc s, warrant		•			cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) o of (D) (Instr. 3,	r Expira	te Exerci ation Da th/Day/Ye			I Amount of Se Security (Instr	curities Underly . 3 and 4)	ing	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securit Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerc		Expiration Date	Title		Amount or Number of Shares			Owned Following Reporte Transac (Instr. 4	ing ed ction(s)		* ')

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

03/05/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*						icker or Trad	0 ,	ol					check all a	nip of Reporting Poplicable)	erson(s) to	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/06/201		ansaction (Mo	onth/Day/Y	'ear)					X	Officer (give title	below) VP, Finance	ce and C		ecify below)
409 ILLINOIS ST.					4. If Amen	idment, Da	te of Original	Filed (Mo	onth/Day	//Year)			6.		or Joint/Group F Form filed by On				
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than O	ne Repo	rting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	ecurities A	cquire	d, Dis	posed of	, or Ben	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transaction	Exe	Deemed cution Date,	3. Transa Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispos	ed Of (D)	Be	Amount of Securiti	· [1	Direct (D	ship Form:) or Indirect	7. Nature of Indirect
					(Month/Day/		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		lowing Reported nsaction(s) (Instr.		(I) (Instr.	4)	Beneficial Ownership (Instr. 4)
Common Stock					03/06/20	18		F		5,8	332(1)	D	\$53.5	55	176,160			D	
Common Stock					03/08/20	18		S		90)6 ⁽²⁾	D	\$52.68	8(3)	175,254			D	
Common Stock					03/08/20	18		S		90)9 ⁽²⁾	D	\$53.4	5(4)	174,345			D	
Common Stock					03/08/20	18		S		7	9(2)	D	\$54.4	7 ⁽⁵⁾	174,266			D	
				Table I			urities Ac s, warrant					icially Own	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)		Securities	of Derivative Acquired (A) o of (D) (Instr. 3	r Expira	e Exerci ation Da h/Day/Ye			d Amount of Se Security (Instr		Inderlying	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securitie Beneficia Owned	re F	0. Ownership form: Direct D) or Indirect I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exerc	isable	Expiration Date	Title		Amour Numbe Shares	er of		Followin Reported Transacti (Instr. 4)	d ion(s)		*)

Explanation of Responses:

1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

2. Shares sold pursuant to a 10b5-1 plan.

- 3. The shares were sold at prices ranging from \$52.10 to \$53.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$53.10 to \$53.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$54.10 to \$54.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/08/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Repo Cotroneo Pat	orting Person*						Ticker or Trad		ol					onship of Reporting F all applicable) Director	Person(s) to	Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 03/13/20		ransaction (Mo	onth/Day/Y	ear)				X	Officer (give title	e below) VP, Finance	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	ate of Original	Filed (Mo	nth/Day	/Year)			6. Indivi	dual or Joint/Group F Form filed by O	• .		
(Street)														Form filed by M	ore than On	e Reporting Person	
SAN FRANCISCO	CA	94	1158														
(City)	(State)	(Zi	ip)														
			Т	able I -	Non-Deri	vative S	ecurities A	cquire	d, Dis	posed of	f, or Ben	eficially Ov	/ned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exe	Deemed ecution Date,	3. Transa Code (Ins		4. Securi (Instr. 3,		ed (A) or Dispos	ed Of (D)	5. Amount of Securing Beneficially Owned Following Reported	D	. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect Beneficial
					(Worlding Bay		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr		(msu. 4)	Ownership (Insti
Common Stock					03/13/20	018		S		5,9	932(1)	D	\$54.61(2)	168,334		D	
Common Stock					03/14/20	015		A		28,	000(3)	A	\$0.00	196,334		D	
Common Stock					03/15/20	018		M		14	1,000	A	\$19.39	210,334		D	
Common Stock					03/15/20	018		M		22	2,094	A	\$29.66	232,428		D	
Common Stock					03/15/20	018		S		22,	290(1)	D	\$52.23(4)	210,138		D	
Common Stock					03/15/20	018		S		13,	804(1)	D	\$53.08(5)	196,334		D	
				Table			curities Acc ls, warrant					icially Own	ed				
Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	action Code	Securities	r of Derivative Acquired (A) o of (D) (Instr. 3	or Expira	e Exerci ition Da n/Day/Ye			d Amount of Se Security (Instr	curities Underly 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficial Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Insti
	Security			Code	v	(A)	(D)	Date Exerc		Expiration Date	Title		Amount or Number of Shares		Following Reported Transactio (Instr. 4)		7
Stock Option (Right to Buy)	\$53.75	03/14/2018		A		38,000		(0	5)	03/14/2028	Com	nmon Stock	38,000	\$0.00	38,000) D	
Stock Option (Right to Buy)	\$29.66	03/15/2018		М			22,094	(0	5)	03/04/2025	Com	nmon Stock	22,094	\$0.00	20,042	2 D	
Stock Option (Right to Buy)	\$19.39	03/15/2018		М			14,000	(0	5)	02/22/2026	Com	nmon Stock	14,000	\$0.00	46,000) D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$54.15 to \$55.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. Represents the grant of restricted stock units. Twenty-five percent of the restricted stock units vest on March 6, 2019, and the remainder vests in equal amounts quarterly thereafter for the following three years.
- 4. The shares were sold at prices ranging from \$51.70 to \$52.675. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$52.70 to \$53.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years,

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

03/15/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*				FIBRO	<u>GEN</u>	nd Ticker or Trace INC [FGEN]						onship of Reporting all applicable) Director	Person(s)	to Issuer	r 10% Owr	ier
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 05/21/20		t Transaction (M	onth/Day/Yea	ar)				X	Officer (give t	tle below) SVP, Fina	ance and	` '	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Origina	Filed (Mont	h/Day/	/Year)			6. Indivi	dual or Joint/Group Form filed by				
(Street) SAN FRANCISCO	CA	94	158											Form filed by	More than (One Rep	oorting Person	
(City)	(State)	(Zi	p)															
			Т	able I - I	Non-Deri	ivative	Securities A	cquired,	Disp	osed of	, or Ben	eficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		2A. Deemed Execution Date, f any	3. Transacti Code (Instr		4. Securit (Instr. 3,		ed (A) or Dispos	ed Of (D)	5. Amount of Secu Beneficially Owner Following Report	d		ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Day		(Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (In:		(i) (iiist	.,)	Ownership (Instr.
Common Stock					05/21/2	018		М		7,	987	A	\$19.39	239,291	1)		D	
Common Stock					05/21/2	018		M		7,	,000	A	\$25.4	246,291	1)		D	
Common Stock					05/21/2	018		S		14,9	987(2)	D	\$55.04 ⁽³⁾	231,304	1)		D	
				Table I			ecurities Ac			,		•	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securit	ber of Derivative ies Acquired (A) ed of (D) (Instr. 3 5)	or Expiration	on Dat			d Amount of Se Security (Instr.		8. Price of Derivative Security (Ins	Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisa	ıble i	Expiration Date	Title		Amount or Number of Shares		Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)		4)
Stock Option (Right to Buy)	\$19.39	05/21/2018		M			7,987	(4)		02/22/2026	Com	mon Stock	7,987	\$0.00	38,0	013	D	
Stock Option (Right to Buy)	\$25.4	05/21/2018		M	7,000 (4) 03/08/2027 Common Stock							7,000	\$0.00	58,0	000	D		

Explanation of Responses:

- 1. Includes 1,420 shares purchased through the Issuer's ESPP on May 15, 2018.
- 2. Shares sold pursuant to a 10b5-1 plan.
- 3. The shares were sold at prices ranging from \$55.00 to \$55.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

05/23/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep	porting Person*					lame and Tio		ng Symbol						tionship of R all applicab	ble)	erson(s) to		% Owner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/01/201	Earliest Tran	nsaction (Mo	nth/Day/Yea	r)				X	Office	er (give title	,	Otl nce and CFO	ner (specify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	e of Original	Filed (Month	/Day/Ye	ear)			6. Indi	Form	filed by On	e Reportir	•	,
(Street) SAN FRANCISCO	CA	94	158											Form	filed by Mc	ore than Oi	ne Reporting Pe	rson
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Dispo	sed of, o	r Bene	ficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day/	Execu		3. Transaction Code (Instr.		4. Securities (Instr. 3, 4 aı		d (A) or Dispos	ed Of (D)	Beneficial	nt of Securit Illy Owned g Reported	·	6. Ownership Fo Direct (D) or Indi (I) (Instr. 4)	
					(h/Day/Year)	Code	·	Amount		(A) or (D)	Price		on(s) (Instr.		(.) (Ownership 4)
Common Stock					06/01/20)18		F		993(1	1)	D	\$54.05		230,311		D	
Common Stock					06/04/20)18		M		6,013	3	Α	\$19.39		236,324		D	
Common Stock					06/04/20)18		S		6,013	(2)	D	\$55.16 ⁽³⁾		230,311		D	
				Table I		tive Secu outs, calls		•	•			cially Own	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A) o		n Date			Amount of Se Security (Instr.		Deri	rice of ivative urity (Instr.	9. Number derivative Securities Beneficia	e Form: Di	rect Indirect direct Beneficial
	Security			Code	v	(A)	(D)	Date Exercisal		piration te Ti	tle		Amount or Number of Shares			Followin Reported Transacti (Instr. 4)	ion(s)	
Stock Option (Right to Buy)	\$19.39	06/04/2018		M			6,013	(4)	02	/22/2026	Comn	non Stock	6,013		\$0.00	32,00	00 D	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Shares sold pursuant to a 10b5-1 plan.
- 3. The shares were sold at prices ranging from \$55.00 to \$55.38. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person*					Name and Ti		ng Symbol					5. Relati (Check a	all ap	p of Reporting Policable)	erson(s) t	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/06/20	f Earliest Tra 18	nsaction (Mo	nth/Day/Yea	·)				X		Officer (give title	below) VP, Fina	ance and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Month	/Day/Y	ear)			6. Indivi		or Joint/Group F Form filed by On	٠.		,	
(Street) SAN FRANCISCO	CA	94	158											F	Form filed by Mo	ore than C	One Rep	oorting Person	
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Deri	ivative Se	curities A	cquired,	Dispo	sed of	f, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	ution Date,	3. Transaction Code (Instr.		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	Ben	mount of Securit eficially Owned owing Reported	ies		ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Day		th/Day/Year)	Code		Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (iiist	1. 4)	Ownership (Instr. 4)
Common Stock					06/06/2	018		F		2,2	277(1)	D	\$56.6		228,034			D	
Common Stock					06/08/2	018		S		1,0)11 ⁽²⁾	D	\$55.55		227,023			D	
				Table I		ative Secu puts, calls						cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative equired (A) o f (D) (Instr. 3,	6. Date Expiratio (Month/Da	n Date			Amount of Se Security (Instr.	curities Underly 3 and 4)	ing	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securiti Benefic	ve ies	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisat		kpiration ate	Title		Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4)	ed ction(s)		4)

Explanation of Responses

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/08/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

** Signature of Reporting Person

Date

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

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FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

l	OMB APPROVAL	
	OMB Number:	3235-0287
	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person*					Name and Tide GEN INC									nship of Reporting P applicable) Director	erson(s) t		10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/13/201	Earliest Trar	nsaction (Mo	nth/Day/Ye	ar)					X	Officer (give title		nce and CFO		ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	of Original	Filed (Mont	th/Day/	Year)			6	. Individu X	ual or Joint/Group F Form filed by Or	ie Reporti	ing Person	,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than C	one Reporting	Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Sed	curities A	cquired,	Disp	osed of	, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day	Execu		3. Transact Code (Insti		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D	´ E	5. Amount of Securit Beneficially Owned Following Reported		6. Ownership Direct (D) or I (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(h/Day/Year)	Code	v	Amount		(A) or (D)	Price	1	Transaction(s) (Instr. 4)		(.) (Ownership (Instr. 4)
Common Stock					06/13/20	018		S		2,3	319(1)	D	\$5′	7.7	224,704		D		
Common Stock					06/14/20	018		М		7,	,750	A	\$2:	5.4	232,454		D		
Common Stock					06/14/20	018		S		7,7	750(1)	D	\$6	0	224,704		D		
				Table I		tive Secu outs, calls		•	•			cially Own ies)	ied						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number o Securities A Disposed of 4 and 5)	cquired (A) o	r Expirati	on Date			d Amount of Se Security (Instr			g 8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	ve Form	wnership Direct Indirect str. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amou Numb Share	er of		Followin Reporte Transact (Instr. 4)	d tion(s)		, , , , , , , , , , , , , , , , , , ,
Stock Option (Right to Buy)	\$25.4	06/14/2018		M			7,750	(2)	(03/08/2027	Com	mon Stock		7,750	\$0.00	50,2	50	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

06/15/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Rep Cotroneo Pat	orting Person*						cker or Tradi	0 ,						onship of Reporting F all applicable) Director	erson(s) to)% Owne	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/04/20		nsaction (Mo	nth/Day/Yea	r)				X	Officer (give title	,	Once and CFO	ther (spe	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Month	/Day/Ye	ear)			6. Individ	dual or Joint/Group F Form filed by Or	٠,		ine)	
(Street)														Form filed by Mo	ore than Or	ne Reporting P	erson	
SAN FRANCISCO	CA	94	158															
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Dispo	sed of,	or Bene	eficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact Date	Exec		3. Transaction Code (Instr.		4. Securit (Instr. 3, 4		d (A) or Dispos	ed Of (D)	5. Amount of Securit Beneficially Owned	[6. Ownership Fo		7. Nature of Indirect
					(Month/Day	/Year) if any (Mon	th/Day/Year)	Code	,	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr 4)		i) (Instr. 4)		Beneficial Ownership (Instr. 4)
Common Stock					09/04/2	018		F		99	4 ⁽¹⁾	D	\$61.05	223,710		D		
Common Stock					09/06/2	018		F		2,2	77 ⁽¹⁾	D	\$57.3	221,433		D		
				Table I			irities Acc s, warrant	. ,	•	,		cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative acquired (A) o f (D) (Instr. 3,		n Date			I Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficia Owned	Form: D s (D) or Ir	irect idirect . 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisal		piration te	Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)	ĭI		4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/06/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Cotroneo Pat	Name and Address of Reporting Person* Cotroneo Pat							2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)										10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/10/20		nsaction (Mor	th/Day/Year)				X	С	officer (give title	,	ance and	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	Filed (Month	Day/Ye	ar)			6. Individ		r Joint/Group Form filed by On	• .		,	
	CA (State)	94 (Zi	158											F	orm filed by Mo	re than (One Rep	orting Person	
	<u> </u>			able I - I	l Non-Deri	vative Sec	curities A	quired, [Dispos	sed of,	or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transact	Execu	ution Date,	3. Transactio Code (Instr.		. Securiti Instr. 3, 4		d (A) or Dispos		Bene	nount of Securiti	es	Direct (ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		h/Day/Voor)	Code	A	Amount		(A) or (D)	Price		owing Reported saction(s) (Instr.	3 and	(I) (Instr	. 4)	Ownership (Instr. 4)
Common Stock					09/10/2	018		S		1,01	11(1)	D	\$57.35		220,422			D	
				Table I		ntive Secu puts, calls			•			cially Own es)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Securities Ad Disposed of 4 and 5)	cquired (A) or	6. Date Ex Expiration (Month/Da	Date			Amount of Se Security (Instr.	curities Underly 3 and 4)	Ĭ	8. Price of Derivative Security (Instr. 5)	9. Numl derivati Securiti Benefic Owned	ve ies	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisab		oiration e	Title		Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ed ction(s)		*)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/12/2018

Date

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person [*]						Ticker or Trad		ol					tionship of Repo all applicable) Director	rting Person(s) to Issuei	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/12/20		Transaction (Mo	onth/Day/Y	ear)				X		ve title below	inance and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, [Date of Original	Filed (Mo	nth/Day	/Year)			6. Indiv	idual or Joint/G Form filed	roup Filing (0 by One Rep		,	
(Street) SAN FRANCISCO	CA	94	158											Form filed	by More tha	n One Rep	orting Person	
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	ivative	Securities A	Acquired	d, Disp	posed of	f, or Ben	eficially O	wned					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	E	A. Deemed xecution Date, any	3. Transa Code (Ins		4. Securi		ed (A) or Dispo	sed Of (D)	5. Amount of 3 Beneficially 0 Following Re	wned		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		any Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s			r. 4)	Ownership (Instr. 4)
Common Stock					09/12/2	018		M		10),500	A	\$2.9	230	,922		D	
Common Stock					09/13/2	.018		S		2,3	318(1)	D	\$59.5	228	,604		D	
				Table I			ecurities Ac alls, warrant						ned					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative es Acquired (A) o d of (D) (Instr. 3	or Expira	e Exercis ition Dat n/Day/Ye			d Amount of S Security (Inst	ecurities Underl r. 3 and 4)	ying 8. Price Derivativ Security 5)	re deriv (Instr. Secu	rities ficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exerci		Expiration Date	Title		Amount or Number of Shares		Folio Repo	owing orted saction(s)		
Stock Option (Right to Buy)	\$2.9	09/12/2018		M			10,500	(2	2)	06/24/2020	Com	ımon Stock	10,500	\$0.0	00 2	29,500	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/14/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

** Signature of Reporting Person

Date

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	orting Person [*]						Ticker or Trad	0 ,						onship of Repo all applicable) Director	orting Pe	erson(s) to Is	ssuer 10% Ow	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/03/20		ransaction (Mo	onth/Day/Ye	ear)				X	Officer (g		,	Other (spee and CFO	pecify below)
409 ILLINOIS ST.					4. If Amer	ndment, D	ate of Original	Filed (Mor	nth/Day	/Year)			6. Indivi		•	ling (Check Reporting	Applicable Line) Person	
(Street)														Form filed	by Mor	e than One	Reporting Person	
SAN FRANCISCO	CA	94	158															
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative S	ecurities A	cquired	, Disp	osed of	f, or Bene	eficially Ov	/ned					
1. Title of Security (Instr. 3)					2. Transact Date	Ex	Deemed ecution Date,	3. Transac Code (Inst		4. Securi (Instr. 3,		d (A) or Dispos	sed Of (D)	5. Amount of Beneficially (Owned	Dir	Ownership Form: rect (D) or Indirect	7. Nature of Indirect
					(Month/Day		ny onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Re Transaction(s 4)			(Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					12/03/20	018		F		99	93(1)	D	\$43.93	22'	7,611		D	
Common Stock					12/06/20	018		F		2,2	277 ⁽¹⁾	D	\$40.93	22:	5,334		D	
				Table I			urities Ac ls, warrant			,		cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	r of Derivative Acquired (A) of of (D) (Instr. 3	or Expirat	ion Dat			I Amount of Se Security (Instr.	curities Underly 3 and 4)	ving 8. Price Derivati Security 5)	ve (Instr.	9. Number derivative Securities Beneficially	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares			Owned Following Reported Transaction (Instr. 4)	n(s)	4)

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/06/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ing Person [*]					Name and Tio		g Symbol						ship of Repor applicable) Director	ing Person(s) to Issue	er 10% Owr	ner
l ` ′	(First)	(M	iddle)		3. Date of 12/18/20	f Earliest Trar 18	nsaction (Mon	th/Day/Yea	ar)				X	Officer (giv		inance an	Other (sp	ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original F	Filed (Mont	th/Day/	Year)			6. Individ	al or Joint/Gr Form filed			,	
	CA		158											Form filed	by More tha	n One Re	porting Person	
(City)	(State)	(Zi		able I - I	Non-Deri	vative Se	curities A	auired.	Disp	osed of	f. or Bene	eficially Ow	ned					
1. Title of Security (Instr. 3)					2. Transact	Execu	ution Date,	3. Transact Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	` '	5. Amount of S Beneficially Ov	ned	Direct	ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		h/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Following Rep Fransaction(s) I)		(I) (Ins	tr. 4)	Ownership (Instr. 4)
Common Stock					12/18/2	018		S ⁽¹⁾		3	,330	D	\$41.1	222,	004		D	
				Table I		ntive Secu puts, calls			•			cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) or (D) (Instr. 3,	6. Date I Expiration (Month/I	on Date	е		I Amount of Se Security (Instr.	curities Underlyir 3 and 4)	8. Price of Derivative Security (5)	nstr. Secu	rities ficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Folio	owing orted saction(s)		·*/

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

12/20/2018 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat				cker or Tradi	0 ,						k all ap	ip of Reporting Peoplicable) Director	erson(s) t	to Issuer	10% Own	er			
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 02/28/20		nsaction (Mo	nth/Day/Yea	ar)						Officer (give title	below) VP, Fina	ince and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	e of Original	Filed (Mont	h/Day/	/Year)					or Joint/Group Fi Form filed by On				
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	re than C	One Repo	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	f, or Ben	eficially O	wned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec		3. Transacti Code (Instr.		4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ber	Amount of Securiti neficially Owned lowing Reported			rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(monta // Duy		th/Day/Year)	Code	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.			. 4)	Ownership (Instr. 4)
Common Stock					02/28/20)19		M		14	1,787	A	\$29.66		267,891			D	
Common Stock					02/28/20)19		S		14,	787 ⁽¹⁾	D	\$60.0792(2)	253,104			D	
				Table I			rities Acc					icially Owr ties)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) (Month/Day/Year) (Month/Day/Year) 7. Title and Amount of Security (Instr. 3 and Title Amount of Securit									8. Price of Derivative Security (Instr.		9. Numb derivativ Securitie Benefici Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Following Reporte Transact (Instr. 4)	ed tion(s)		 ',
Stock Option (Right to Buy)	\$29.66	02/28/2019		M			14,787	(3) 03/04/2025 Common Stock			14,78	14,787 \$0.00		5,255		D			

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$60.00 to \$60.36. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/01/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	orting Person [*]					Ticker or Trad	0 ,	l				ionship of Reportii all applicable) Director	g Person(s) to Issuer	10% Own	er		
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/04/20		ransaction (Mo	onth/Day/Ye	ear)				X	Officer (give	SVP, Fir	nance and		ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, D	ate of Original	nth/Day	/Year)		6. Indivi	dual or Joint/Gro			,			
(Street)														Form filed by	More than	One Rep	orting Person	
SAN FRANCISCO	CA	94	158															
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	Non-Derivative Sec		ities Acquired, Dispo		osed of	, or Bene	eficially Ov	/ned					
1. Title of Security (Instr. 3)					Date E		Execution Date,		tion tr. 8)	4. Securi (Instr. 3,		d (A) or Dispos	sed Of (D)	5. Amount of See Beneficially Own	ned Dire		ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		ny onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Repo Transaction(s) (I 4)		(I) (Instr	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					03/04/20	019		F		69	93(1)	D	\$58.69	558.69 252,411			D	
Common Stock					03/06/20	019		F		5,2	242(1)	D	\$55.58	\$55.58 247,169			D	
				Table I			urities Ac ls, warrant	. ,		,		cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	r of Derivative Acquired (A) of of (D) (Instr. 3	Exercis ion Dat Day/Ye		7. Title and Derivative	curities Underly 3 and 4)	8. Price of Derivative Security (Ir 5)	9. Nun deriva Securi Benefi Owned	tive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.		
	Derivative Security			Code	v	(A)	(D)		Expiration Date	Title	Amount or Number of Shares	r		ving ted action(s) 4)		4)		

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

03/06/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
١	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

. Name and Address of Reporting Person* Cotroneo Pat						Name and Tion OGEN INC		g Symbol					nship of Ro Il applicabl Directo	,	erson(s) to	o Issuer	10% Own	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 03/19/20	f Earliest Trar 19	nsaction (Mon	th/Day/Year)				X	Officer	r (give title	below) VP, Finar	nce and		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Month	/Day/Yea	ar)			6. Individ	Form f	filed by One	e Reporti	ng Perso		
(Street) SAN FRANCISCO	CA	94	158										Form f	filed by Mo	re than O	ne Repo	orting Person		
(City)	(State)	(Zi	ablo I - l	Non-Dori	vativo So	curities A	equired [Dienos	end of	or Bono	ficially Ov	mod.							
1. Title of Security (Instr. 3)			<u> </u>	45.51				3. Transactio	n 4		ies Acquire	d (A) or Dispos	sed Of (D)	5. Amount Beneficiall Following				rship Form: 0) or Indirect	7. Nature of Indirect Beneficial
					(Monthiba)		h/Doy/Voor)	ode V Amount		Amount	(A) or (D)		Price	Transaction(s) (Insti			(i) (iiioti.	- 1/	Ownership (Instr. 4)
Common Stock					03/19/2	019		S		7,60	65(1)	D	\$55.41	2	239,504			D	
	Table I	II - Derivative Securities Act (e.g., puts, calls, warrant								ed									
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	4. Transa (Instr. 8)	ction Code 5. Number of Deriva Securities Acquired Disposed of (D) (Ins 4 and 5)		cquired (A) or	6. Date Ex Expiration (Month/Da	Date			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	Deriv	vative	9. Number of derivative Securities Beneficially		10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.		
	Code	V (A) (D)		(D)	Date Exercisab		expiration Date Title			Amount or Number of Shares	mber of		Owned Following Reported Transaction (Instr. 4)			4)			

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

03/20/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Repor Cotroneo Pat		FIBRO	Name and Tio	[FGEN]						ship of Reporting P applicable) Director	erson(s) t	to Issuer	10% Own	er				
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 06/06/20	f Earliest Trar 19	nsaction (Mor	th/Day/Ye	ear)				X	Officer (give title	below) VP, Fina	ance and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original I	iled (Mon	ith/Day/	/Year)			6. Individ	al or Joint/Group F Form filed by Or	ne Report	ing Perso	on	
(Street) SAN FRANCISCO	CA	94	1158											Form filed by Mo	ore than C	One Repo	orting Person	
(City)	(State)	'abla I	Nam Davi	inadina Car			Diam		. av Dana	ficially Ov								
1. Title of Security (Instr. 3)			<u>'</u>	able I -	2. Transact Date (Month/Day	tion 2A. De	eemed ution Date,	3. Transact	tion	1	ities Acquire	d (A) or Dispos	ed Of (D)	5. Amount of Securit Beneficially Owned Following Reported			rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII)Day		h/Day/Vaar\	Code	v	Amount		(A) or (D)	Price	ransaction(s) (Instr.				Ownership (Instr. 4)
Common Stock					06/06/2	019		F		3,1	144 ⁽¹⁾	D	\$38.31	253,978(2)			D	
				Table I		ntive Secu puts, calls		-	•			cially Own ies)	ed					
1. Title of Derivative Security (Instr. 3)								6. Date Exercisable Expiration Date (Month/Day/Year)		е		Amount of Se Security (Instr.	curities Underlyir 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic	ve ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Expira		Expiration No.		Amount or Number of Shares	Folio Repo Trans		ollowing eported ransaction(s) nstr. 4)		- *)	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 618 shares acquired on May 15, 2019 through the Issuer's Employee Stock Purchase Plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/07/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat				cker or Tradii	ng Symbol					ationship of Reporting Person(s) to Iss k all applicable) Director			to Issuer	suer 10% Owner					
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/18/20		nsaction (Mo	nth/Day/Ye	ear)				X		ficer (give title	below) VP, Fina	ince and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mon	ith/Day	Year)		6. Individ		Joint/Group Fi	٠,	• • •	,		
	CA		158											For	rm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi		'abla l	Non Dori	votivo Co	ourition A		Dier		i or Pone	ficially Ov	mad						
1. Title of Security (Instr. 3)			<u> </u>	ubic i - i	2. Transaction Date (Month/Day/Year) if any			3. Transac Code (Inst	tion	1	ties Acquire	d (A) or Dispo		Benefi	ount of Securiti icially Owned ving Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Ab/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)			(.) (,	Ownership (Instr. 4)
Common Stock					06/18/2	019		S		3,2	201(1)	D	\$43.12	2 250,777				D	
				Table I	II - Derivative Securities Ac (e.g., puts, calls, warran			•				•	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative Acquired (A) of f (D) (Instr. 3,		ion Dat			Amount of Se Security (Instr	curities Underlyi 3 and 4)	8. Price of Derivative Security (Instr		9. Numb derivativ Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	Date Expiration N							Amount or Number of		Owned Following Reported Transaction(s) (Instr. 4)					

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/20/2019 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

I. Name and Address of Reporting Person* Cotroneo Pat						Name and Tion OGEN INC		g Symbol					l applica	ship of Reporting Person(s) to Iss applicable) Director		to Issuer	10% Own	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o	f Earliest Trar 19	nsaction (Mon	th/Day/Ye	ar)				X	Offic	er (give title	,	ince and		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Mont	th/Day/	Year)			6. Individ	Form	oint/Group Fi n filed by One	e Report	ing Perso	on	
(Street) SAN FRANCISCO	CA	94	158											Form	n filed by Mo	re than (One Repo	orting Person	
(City)	(State)	(Zi																	
			Т	able I - I	Non-Deri	vative Sec	curities A	quired,	, Disp	osed of	i, or Bene	ficially Ov	ned						
1. Title of Security (Instr. 3)					Date			3. Transact Code (Insti		4. Securi (Instr. 3,		d (A) or Dispos	` ′	Benefici	int of Securiti	es	Direct (E	rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		h/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)			and (I) (Instr. 4)		Ownership (Instr. 4)
Common Stock					09/06/2	019		F		3,1	144 ⁽¹⁾	D	\$41.68	247,633				D	
				Table I		ntive Secu puts, calls						cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Derivative Securities Acquired (A) of Disposed of (D) (Instr. 3, 4 and 5)		6. Date I Expirati (Month/I	on Date			Amount of Se Security (Instr.	curities Underlyi 3 and 4)	ying 8. Price of Derivative Security (Inst		9. Numb derivati Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Expir Exercisable Date		Expiration Nur		Amount or Number of Shares	Follo Repo Trans		Followi Reporte	eported ansaction(s)		+ ,	

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

09/10/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]				1	Name and Ti OGEN INC	cker or Tradio	ng Symbol	ı				5. Relation (Check a		,	erson(s) t	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(N	liddle)		3. Date o		nsaction (Mo	nth/Day/Ye	ear)				X	Office	cer (give title	below) VP, Fina	nce and	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mon	nth/Day	/Year)			6. Individ	Form	oint/Group Fi m filed by One	e Reporti	ing Perso	on	
(Street) SAN FRANCISCO (City)	CA (State)		i158											Form	m filed by Mo	re than C	One Repo	orting Person	
			7	Γable I -	Non-Der	ivative Se	curities A	cquired	l, Dis _l	posed of	f, or Bene	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transac Date	Exec		3. Transac Code (Inst		4. Secur (Instr. 3,		d (A) or Dispos	sed Of (D)	Benefici	unt of Securiti		Direct (I	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Da		h/Daw/Vaan	Code	v	Amount		(A) or (D)	Price		ng Reported ction(s) (Instr.		(I) (Instr	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					09/17/2	019		S		3,	201(1)	D	\$41.38		244,432			D	
				Table I		- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities A	of Derivative acquired (A) of f (D) (Instr. 3,		tion Da			I Amount of Se Security (Instr	curities Underlyi 3 and 4)	Dei		9. Numb derivativ Securitie Benefici	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	Date Expiration No.							Amount or Number of Shares			Owned Followin Reporte Transact (Instr. 4)	tion(s)		4)	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/18/2019

Date

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]						cker or Tradir	g Symbol					5. Relatio (Check a	ll appli	of Reporting Peicable)	erson(s)	to Issuer	10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 12/06/20		nsaction (Mor	th/Day/Ye	ar)				X		ficer (give title	below) VP, Fina	ince and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	iled (Mont	th/Day	/Year)			6. Individ		Joint/Group Form filed by On	٠,	• • •	,	
(Street) SAN FRANCISCO	CA	94	158											Fo	orm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi							<u> </u>		, ,	<i></i>							
1. Title of Security (Instr. 3)			I	able I -	2. Transac			3. Transact	•	_	•	d (A) or Dispos		E Ame	ount of Securiti	ioo	6 Owns	ership Form:	7. Nature of
1. Title of Security (illstr. 3)					Date (Month/Day	Exec	ution Date,	Code (Insti		(Instr. 3,		u (A) of Dispos	` ′	Benefi	icially Owned ving Reported	162		D) or Indirect	Indirect Beneficial
					(th/Day/Vaan	Code	v	Amount		(A) or (D)	Price		action(s) (Instr.	3 and	(.) (,	Ownership (Instr. 4)
Common Stock					12/06/2	019		F		3,	144(1)	D	\$47.39		253,788			D	
				Table I			rities Acq s, warrants					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative acquired (A) or f (D) (Instr. 3,	6. Date I Expirati (Month/I	ion Dat			I Amount of Se Security (Instr	curities Underlyi 3 and 4)	S	3. Price of Derivative Security (Instr. 5)	9. Numl derivati Securiti Benefic Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	Date Expiration							Amount or Number of Shares			Followi Reporte Transac (Instr. 4	ed tion(s)			

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

12/09/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

						01 360	ction 30(h) of th	e ilivesillei	ii Coiii	ipally Act C	JI 1540						
Name and Address of Rep Cotroneo Pat	orting Person [*]						Ticker or Trad	0 ,						nship of Reporting P applicable) Director	erson(s) to I	ssuer 10% Owr	ıer
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/20/20		Transaction (M	onth/Day/Ye	ar)				X	Officer (give title	below) VP, Finance	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, [Date of Origina	Filed (Mon	th/Day/	/Year)			6. Individu	al or Joint/Group F Form filed by Or	• (,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than One	e Reporting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	on-Derivative Securities Acquired, Disposed of, or Beneficially Owned											
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	A. Deemed cecution Date, any	3. Transact Code (Instr		4. Securi (Instr. 3,	ities Acquire 4 and 5)	` ′ [5. Amount of Securit Beneficially Owned Following Reported	Di	Ownership Form: irect (D) or Indirect (Instr. 4)	7. Nature of Indirect Beneficial	
					(oazu)		lonth/Day/Year)	Code	v	Amount		(A) or (D)	Price .	Fransaction(s) (Instr.		(incur 4)	Ownership (Instr 4)
Common Stock					12/20/20	12/20/2019		M		18	3,000	A	\$3.5	271,788		D	
Common Stock					12/20/20)19		M		21	1,000	A	\$5.95	292,788		D	
Common Stock					12/20/20)19		M		17	7,254	A	\$14.575	310,042		D	
Common Stock					12/20/20)19		S		46,	727(1)	D	\$45.51 ⁽²⁾	263,315		D	
Common Stock					12/20/20)19		S	s 12,729 ⁽¹⁾ D					250,586		D	
				Table I			curities Ac						d				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative es Acquired (A) d of (D) (Instr. 3	or Expirati	on Date			d Amount of Sec Security (Instr.	urities Underlyin 3 and 4)	g 8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficially Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr 4)
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)		,
Stock Option (Right to Buy)	\$3.5	12/20/2019		М			18,000	(4)		06/07/2021 Common Stock		mon Stock	18,000	\$0.00	0	D	
Stock Optin (Right to Buy)	\$5.95	12/20/2019		M			21,000	(4)		06/27/2022	27/2022 Common Stock		21,000	\$0.00	0	D	
Stock Option (Right to Buy)	\$14.575	12/20/2019		M			17,254	(4)		03/19/2024 Common Stock		17,254	254 \$0.00		D		

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$44.91 to \$45.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$45.91 to \$46.44. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Fully vested

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/26/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep <u>Cotroneo Pat</u>	orting Person [*]					lame and Tio									nship of Reporting Papplicable) Director	erson(s) to)% Owne	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/06/202	Earliest Trar 20	nsaction (Mo	onth/Day/Yea	ar)					X	Officer (give title	,	once and CFO	ther (spe	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, Date	of Original	Filed (Mont	th/Day/	Year)			6	6. Individu X	ual or Joint/Group F Form filed by On	e Reporti	ing Person	,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than O	one Reporting P	erson	
(City)	(State)	(Zi	p)																
			T	able I -	Non-Deri	vative Sed	curities A	cquired,	Disp	osed of	, or Bene	eficially Ov	wned						
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day/	Execu		3. Transacti Code (Instr		4. Securit (Instr. 3, 4		d (A) or Dispos	sed Of (D	´ E	5. Amount of Securit Beneficially Owned Following Reported		6. Ownership For Direct (D) or Inc (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(h/Day/Year)	Code	v	Amount		(A) or (D)	Price	1	Transaction(s) (Instr. 4)		(,, (,		Ownership (Instr. 4)
Common Stock					03/06/20)20		F		4,8	81(1)	D	\$39	.71	245,705		D		
Common Stock					03/16/20)20		S		9,2	39 ⁽²⁾	D	\$26	5.36	236,466		D		
Common Stock					03/17/20)20		A		40,0	000(3)	A	\$0.	.00	276,466		D		
				Table I		tive Secu outs, calls			•			cially Own ies)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	sction Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)										derlying 8. Price of Derivative Security (Instr. 5)		per of ve Form: I (D) or I (I) (Insti	irect idirect	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amou Numi Share			Owned Followir Reported Transact (Instr. 4)	d tion(s)		
Stock Option (Right to Buy)	\$26.41	03/17/2020		A		66,250		(4)		03/17/2030	Com	mon Stock		66,250	\$0.00	66,2	.50 I		

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Shares sold pursuant to a 10b5-1 plan.
- 3. Represents the grant of restricted stock units. Twenty-five percent of the restricted stock units vest on March 6, 2021, and the remainder vests in equal amounts quarterly thereafter for the following three years.
- 4. Twenty-five percent of the shares subject to the option vests on March 1, 2021, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
١	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ing Person [*]				2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)									nship of Re I applicable Director	e)	erson(s) to	s Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o 06/08/20		nsaction (Mor	th/Day/Yea	ar)				X	Officer ((give title	,	nce and (٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original I	iled (Mont	th/Day/	Year)			6. Individ		iled by One	e Reporti	ng Perso	n	
(Street) SAN FRANCISCO	CA	94	158											Form fil	iled by Mor	re than O	ne Repoi	ting Person	
(City)	(State)	(Zi				0			<u> </u>										
1. Title of Security (Instr. 3)			'	able I -	2. Transac	tion 2A. De	eemed ution Date,	3. Transact Code (Instr	ion	1	ities Acquire	eficially Ov	ed Of (D)	5. Amount o	y Owned		Direct (D	ship Form:	7. Nature of Indirect
					(Month/Day		h/Day/Vaan	Code	v	Amount		(A) or (D)	Price	Following F Transaction 4)			(I) (Instr.	4)	Beneficial Ownership (Instr. 4)
Common Stock					06/08/2	020		F		2,1	156(1)	D	\$33.61	27	74,988(2)			D	
				Table I		ative Secu puts, calls						cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) or (D) (Instr. 3,	6. Date I Expiration (Month/I	on Date	е		Amount of Se Security (Instr.	curities Underlyi 3 and 4)	Deriva	ative rity (Instr.	9. Numb derivativ Securitie Beneficia Owned	e F	0. Ownership orm: Direct D) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	V (A) (D) Date Expiration Date Title							Amount or Number of Shares			Followin Reported Transact (Instr. 4)	ion(s)		- *)	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 678 shares acquired on May 15, 2020 through the Issuer's Employee Stock Purchase Plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/10/2020

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

Date

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]				FIBRO	OGEN IN	cker or Tradir						5. Relation (Check a	ıll app	o of Reporting Pe blicable) birector	erson(s)	to Issuer	r 10% Owr	ner		
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o		nsaction (Mo	nth/Day/Ye	ear)				X	С	officer (give title	below) VP, Fina	ance and	` .	ecify below)		
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mon	ith/Day	/Year)			6. Individ		r Joint/Group Form filed by On	• .		,			
(Street) SAN FRANCISCO	CA		158											F	orm filed by Mo	re than (One Rep	porting Person			
(City)	(State)	(Zi		Table I -	Non-Der	ivative Se	curities A	cquired	, Disp	oosed of	f, or Bene	eficially Ov	/ned								
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exec	ution Date,	3. Transac Code (Inst		4. Securi		d (A) or Dispos	sed Of (D)	Bene	nount of Securiti eficially Owned	es		ership Form: (D) or Indirect	7. Nature of Indirect Beneficial		
					(WIOTICII/Day		Ab/Day/Vaan	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (ilist	1. 4)	Ownership (Instr. 4)		
Common Stock					06/16/2	.020		S		3,9	928(1)	D	\$39.68		271,060			D			
				Table I		- Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)						ed									
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	tion Code S. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securit Derivative Security (Instr. 3 and S)								Ĭ	Derivative Security (Instr. 5) deriv Secu		Derivative Security (Instr. 5) Ge		ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	Date Expiration N							Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)				

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/18/2020

Date

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep	porting Person*						Ticker or Trad		l					nship of Reporting P I applicable) Director	Person(s) to	Issuer	10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 08/07/202		Transaction (Mo	onth/Day/Ye	ear)				X	Officer (give title	,	nce and CFC	٠.	pecify below)
409 ILLINOIS ST.					4. If Amer	ndment, D	Date of Original	Filed (Mon	nth/Day	Year)			6. Individ	ual or Joint/Group F Form filed by Or	• ,		Line)	
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than Or	ne Reporting	Person	
(City)	(State)	(Zi	p)															
			Т	able I - I	Non-Deri	vative \$	Securities A	cquired, Disp		osed of	f, or Bene	eficially Ow	ned					
1. Title of Security (Instr. 3)										I. Securities Acquired (A) or Disposed (Instr. 3, 4 and 5)			5. Amount of Securit Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial	
					lonth/Day/Year)	Code	v	Amount		(A) or (D)	Drica	Transaction(s) (Instr. 4)		(1) (111341. 4)		Ownership (Instr.		
Common Stock					08/07/20	020		М		22	2,554	A	\$19.39	293,614		D		
Common Stock					08/07/20	020		S		22,	554 ⁽¹⁾	D	\$48	271,060		D		
Common Stock					08/11/20)20		M		3,	,750	A	\$19.39	274,810		D		
Common Stock					08/11/20)20		M		3,	,500	A	\$18	278,310		D		
				Table I			curities Ac	. ,		,		•	d					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative es Acquired (A) o d of (D) (Instr. 3	r Expirat	ion Dat			d Amount of Sec Security (Instr.	urities Underlyii 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficia Owned	e Form (D) o	Direct Indirect	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security							Date Exercis		Expiration Date	Title		Amount or Number of Shares		Following Reported Transacti (Instr. 4)	ion(s)		7
Stock Option (Right to Buy)	\$19.39	08/07/2020		M			22,554	(2)		02/22/2026	Com	mon Stock	22,554	\$0.00	9,440	6	D	
Stock Option (Right to Buy)	\$19.39	08/11/2020		М			3,750	(2)		02/22/2026	Com	mon Stock	3,750	\$0.00	5,690	6	D	
Stock Option (Right to Buy)	\$18	08/11/2020		M			3,500	(2)		11/13/2024	Com	mon Stock	3,500	\$0.00	0		D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/11/2020

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep	porting Person*						Ticker or Trad		I					ship of Reporting P applicable) Director	Person(s) to	Issuer	10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/03/202		Transaction (Mo	onth/Day/Ye	ear)				X	Officer (give title	,	nce and CFO	٠.	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment, [Date of Original	Filed (Mor	nth/Day/	Year)			6. Individu	al or Joint/Group F Form filed by Or			e Line)	
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than Or	ne Reportinç	g Person	
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative	Securities A	Acquired, Disp		osed of	f, or Benefici	ally Own	ed					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	A. Deemed xecution Date, any	3. Transac Code (Inst		4. Securi (Instr. 3,	ties Acquired (A) 4 and 5)	or Disposed	E	. Amount of Securit Seneficially Owned following Reported	0	6. Ownership Direct (D) or (I) (Instr. 4)		7. Nature of Indirect Beneficial
							lonth/Day/Year)	Code	v	Amount	(A) c	r (D) Pr	_{ica} 1	ransaction(s) (Instr.		(1) (111341. 4)		Ownership (Instr.
Common Stock					09/03/20	020		M		(537	A	\$29.66	278,947		D		
Common Stock					09/03/20	020		M		5,	,696	A	\$19.39	284,643		D		
Common Stock					09/03/20	020		M		8	,671	A	\$25.4	293,314		D		
Common Stock					09/03/20	020		S		15,	004(1)	D	\$50.91(2)	278,310		D		
				Table I						,	or Beneficiali e securities)	y Owned	I					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative es Acquired (A) o d of (D) (Instr. 3	6. Date Exercisa		е		le and Amount of Securities ative Security (Instr. 3 and 4		8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficia Owned	e Form s (D) o	Ownership n: Direct or Indirect nstr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Following Reported Transactio (Instr. 4)	ĭ					
Stock Option (Right to Buy)	\$29.66	09/03/2020		M			637	(3)		03/04/2025	Common S	tock	637	\$0.00	4,618	8	D	
Stock Option (Right to Buy)	\$19.39	09/03/2020		M			5,696	(3)		02/22/2026	Common S	tock	5,696	\$0.00	0		D	
Stock Option (Right to Buy)	\$25.4	09/03/2020		M			8,671	(4)		03/08/2027	Common S	tock	8,671	\$0.00	41,57	79	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$50.89 to \$51.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

3. Fully vested.

4. Twenty-five percent of the shares subject to the option vests on the first anniversary of the vesting commencement date, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/04/2020

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	Name and Address of Reporting Person* Cotroneo Pat						cker or Tradir	ng Symbol					5. Relatio (Check a	ll appli	of Reporting Pericable)	erson(s)	to Issuer	10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 09/08/20		nsaction (Mor	nth/Day/Ye	ar)				X		ficer (give title	below) VP, Fina	ince and	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mont	th/Day/	Year)			6. Individ		Joint/Group Fi	٠,	• • •	,	
	CA		158											Foi	rm filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Zi			N D	4 0 .			D:		D	£1 - 1 - 11 - 1 O - 1							
1. Title of Security (Instr. 3)				able i -	2. Transaction Date (Month/Day/Year) if any		eemed ution Date,	3. Transact Code (Insti	tion	1	ties Acquire	d (A) or Dispos	ed Of (D)	Benefi	ount of Securiti icially Owned ving Reported	es		ership Form: D) or Indirect	7. Nature of Indirect
					(MOIIIII/Da)		th/Day/Vaan	Code	v	Amount		(A) or (D)	Price		action(s) (Instr.	3 and	(i) (iiisti	. 4)	Ownership (Instr. 4)
Common Stock					09/08/2	020		F		3,0)14 ⁽¹⁾	D	\$42.16		275,296			D	
				Table I			rities Acq , warrants		•			cially Own es)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative cquired (A) or f (D) (Instr. 3,		on Date			Amount of Se Security (Instr	curities Underlyi 3 and 4)	Ĭ D		9. Numb derivati Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	Date Expiration Nu							Amount or Number of Shares			Owned Following Reported Transaction(s) (Instr. 4)				

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/10/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	Name and Address of Reporting Person* Cotroneo Pat						ker or Tradin				5. Relation (Check a	II ap	p of Reporting Pe olicable) Director	erson(s)	to Issuer	10% Own	er		
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/15/20	f Earliest Trar 20	nsaction (Mon	th/Day/Year	-)				X	(Officer (give title	,	ance and	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Month	/Day/\	Year)			6. Individ		or Joint/Group Fi Form filed by On			•	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158												Form filed by Mo	re than (One Rep	orting Person	
(City)	(State)	(Σι		able I - I	 Non-Deri	vative Sec	curities Ac	quired, [Disp	osed of	, or Bene	ficially Ov	/ned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Execu	ition Date,	3. Transactio Code (Instr.		4. Securit		d (A) or Dispos	ed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(WOIIII/Day		h/Dau/Vaan	Code V	'	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(i) (iiisti	4)	Ownership (Instr. 4)
Common Stock					09/15/2	020		S		3,0)70(1)	D	\$43.63		272,226			D	
				Table I		ntive Secu puts, calls	•		•			cially Own es)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number o Securities Ad Disposed of 4 and 5)	cquired (A) or	6. Date Ex Expiration (Month/Da	n Date			Amount of Se Security (Instr.	curities Underly 3 and 4)	ng	8. Price of Derivative Security (Instr. 5)	9. Numi derivati Securiti Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	Date Expiration Date Title							Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)	- ',	

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/17/2020

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	Name and Address of Reporting Person* Cotroneo Pat							2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)										10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/07/20		nsaction (Mo	nth/Day/Ye	ear)				X	C	Officer (give title	,	ance and		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mor	nth/Day	/Year)			6. Individ		or Joint/Group Fi Form filed by On			•	
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158												Form filed by Mo	re than (One Rep	orting Person	
(Oily)	(Otate)	(Δ1		able I - I	 - Non-Derivative Securities Acq		cquired	I, Disp	osed of	, or Bene	ficially Ov	vned							
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Date Execution Date,		3. Transac Code (Ins		4. Securi (Instr. 3,		d (A) or Dispo	sed Of (D)	Ben	mount of Securiti	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(MOIIII/Day		th/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Insti- 4)				4)	Ownership (Instr. 4)
Common Stock					12/07/2	020		F		3,0)14 ⁽¹⁾	D	\$41.99		269,212			D	
				Table I			rities Acc					cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative equired (A) or f (D) (Instr. 3,	Expirat				Amount of Se Security (Instr	curities Underly . 3 and 4)	9. Price of Derivative Security (Instr. 5)		9. Numi derivati Securiti Benefic	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date						Owned Following Reported Transaction(s (Instr. 4)	ing ed ction(s)		- ',

Explanation of Responses:

1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

12/09/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	Name and Address of Reporting Person* <u>Cotroneo Pat</u>						ker or Tradin	g Symbol					nship of Reporti applicable) Director	ng Person(s) to Issue	10% Owr	ner	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 12/15/20	f Earliest Trar <mark>20</mark>	nsaction (Mon	th/Day/Yea	ar)				X	Officer (give		ı) inance and	` .	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original F	iled (Mont	th/Day/	Year)			6. Individ	ial or Joint/Gro Form filed b	y One Rep	orting Per	son	
(Street) SAN FRANCISCO	CA	94	158												y More tha	n One Re _l	porting Person	
(City)	(State)	(Zi	p)															
			Т	able I - I	Non-Der	vative Sec	curities A	quired,	Disp	osed of	, or Bene	ficially Ov	ned					
1. Title of Security (Instr. 3)					2. Transac	Execu	ition Date,	3. Transact Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	` '	5. Amount of Se Beneficially Ow Following Repo	ned	Direct	ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		h/Dau/Vaan	Code	v	Amount		(A) or (D)	Price	Fransaction(s) (Transaction(s) ((I) (Instr. 4)		Ownership (Instr. 4)
Common Stock					12/15/2	020		S		3,0	068(1)	D	\$43.6	266,1	14		D	
				Table I					red, Disposed of, o		ed of, or Beneficially Owned vertible securities)		ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Derivative Securities Acquired (A) o Disposed of (D) (Instr. 3, 4 and 5)		6. Date E Expiration (Month/E	on Date	•		Amount of Se Security (Instr.	curities Underlyir 3 and 4)	g 8. Price of Derivative Security (I 5)	deriv	rities eficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Expiration Exercisable Date			Title		Amount or Number of Shares	- C F F		ed owing orted saction(s) r. 4)		

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/17/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Signature of Reporting Person

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]		1	Name and Tion		g Symbol						nship of Re Il applicable Director	,	erson(s) to	o Issuer	10% Own	er		
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 03/08/20	f Earliest Trai 21	nsaction (Mor	th/Day/Yea	ar)				X	Officer	give title	below) /P, Fina	nce and	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Date	of Original I	iled (Mont	th/Day/	Year)			6. Individ	Form fi	nt/Group Fil	e Reporti	ng Perso	n	
(Street) SAN FRANCISCO	CA	94	158									Form fi	filed by Mor	re than O	ne Repo	rting Person			
(City)	(State)	(Z			Ion-Derivative Securities Acquired, Disposed of, or Beneficially Owned														
			Т	able I - I	Non-Derivative Securities Acquired, Di					osed of	, or Bene	eficially Ov	/ned						
1. Title of Security (Instr. 3)					2. Transaci Date (Month/Day	Exec	ution Date,	3. Transact Code (Instr		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount Beneficially Following				ship Form:) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		h/Day/Vaan	Code	v	Amount		(A) or (D)	Price	Transastian(a) (lua			(I) (INST.	4)	Ownership (Instr. 4)
Common Stock					03/08/2	021		F		5,6	557(1)	D	\$33.37	282,187		D		D	
				Table I			rities Acquired, Disposed of, or Beneficial , warrants, options, convertible securities)				ed								
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) or (D) (Instr. 3,	6. Date E Expiration (Month/E	on Date	sable and 7. Title and Amount of Securitie te Derivative Security (Instr. 3 and				8. Price of Derivative Security (Instr. 5)		9. Numb derivativ Securitie Benefici	re F es (IO. Ownership Form: Direct D) or Indirect I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisa	Expiration Numb		Amount or Number of Shares	Ow Fol Rej Tra	Followin Reported	Owned Following Reported Fransaction(s)					

Explanation of Responses:

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact
** Signature of Reporting Person

03/10/2021

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{1.} Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]				Name and Tio		g Symbol	I				5. Relati (Check a	all app	o of Reporting Pe blicable)	erson(s) t	to Issuer	10% Own	or.	
(Last)	(First)	(M	iddle)		3. Date of 06/07/20	f Earliest Trar 21	nsaction (Mor	ith/Day/Ye	ear)				X		Officer (give title	below) VP, Fina	nce and	Other (sp	ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original I	iled (Mon	nth/Day	/Year)			6. Individ		or Joint/Group F	٠,		,	
(Street) SAN FRANCISCO	CA	94	158									F	Form filed by Mo	re than (One Repo	orting Person			
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Deri	n-Derivative Securities Acquired, Disposed of, or Benefic							vned						
1. Title of Security (Instr. 3)					2. Transact Date	Execu	ution Date,	3. Transac Code (Inst		4. Securi (Instr. 3,		d (A) or Dispo	sed Of (D)	Bene	mount of Securiti eficially Owned	es	Direct (I	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		h/Day/Vaan	Code	v	Amount		(A) or (D)	Price		owing Reported saction(s) (Instr.	3 and	(I) (Instr	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					06/07/2	021		F		2,1	141(1)	D	\$22.9	280,730(2)				D	
				Table I		Derivative Securities Acquired, Disposed of, or Beneficia (e.g., puts, calls, warrants, options, convertible securities					•	ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) or (D) (Instr. 3,	6. Date Expirat (Month/	ion Dat			Amount of Se Security (Instr	curities Underly . 3 and 4)	-	8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	Date Expiration								Amount or Number of Shares	r	Owned Following Reported Transaction(s) (Instr. 4)	tion(s)		4)	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Includes 684 shares acquired on May 14, 2021 through the Issuer's Employee Stock Purchase Plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/09/2021

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

othy Pacini, Attorney-in-fact

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Report Cotroneo Pat	ting Person [*]				FIBRO	OGEN IN	cker or Tradir						5. Relation (Check a	all ap	p of Reporting Popicable) Director	erson(s)	to Issuer	r 10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o 06/15/20		nsaction (Mo	nth/Day/Ye	ear)				X	(Officer (give title	,	ance and	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	Filed (Mon	ith/Day	/Year)			6. Indivi		or Joint/Group F Form filed by On	• .		,	
	CA		158												Form filed by Mo	re than (One Rep	porting Person	
(City)	(State)	(Zi		Table I -	Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned						vned								
1. Title of Security (Instr. 3)					2. Transac Date (Month/Day	Exec	ution Date,	3. Transac Code (Inst		4. Securi		d (A) or Dispos	sed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	es		ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(MOTICI/Day		Ab/Day/Vaan	Code	v	Amount		(A) or (D)	Price	Tunnanation(a) (luni			(i) (ilist	1. 4)	Ownership (Instr. 4)
Common Stock					06/15/2	.021		S		4,0	053(1)	D	\$25.62		276,677			D	
				Table I	I - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)					ed									
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	action Code 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of S Derivative Security (Instr. 4)									ing	8. Price of Derivative Security (Instr. 5) 9. Num derivat Securit Securit Benefic		ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	Date Expiration N								Amount or Number of Shares			Owned Followi Reporte Transac (Instr. 4	ing ed ction(s)		4)

Explanation of Responses:

1. Shares sold pursuant to a 10b5-1 plan.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

06/17/2021

Date

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

EXHIBIT DDD

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Schoeneck James A	ing Person [*]				2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]										ship of Reporting Papplicable) Director	erson(s) to	o Issuer	10% Own	or.
(Last)	(First)	(M	iddle)		3. Date of 06/22/20	Earliest Trai	nsaction (Mo	nth/Day/Ye	ar)					X	Officer (give title	below)			ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Amer	ndment, Date	e of Original	Filed (Mon	th/Day	/Year)			6.	Individua X	al or Joint/Group F Form filed by On Form filed by Mo	ie Reporti	ing Perso	on	
(Street) SAN FRANCISCO	CA	94	158															3	
(City)	(State)	(Zi _l	p)																
			Т	able I -	- Non-Derivative Securities Ac		cquired	, Disp	osed of	f, or Bene	eficially Ov	wned							
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	eemed ution Date,	3. Transaction Code (Instr. 8		4. Secur (Instr. 3,		d (A) or Dispo	sed Of (D)	В	5. Amount of Securities Beneficially Owned Following Reported			rship Form: 0) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		th/Day/Year)	Code	v	Amount		(A) or (D)	Price		ransaction(s) (Instr.		(I) (INST.	. 4)	Ownership (Instr. 4)
Common Stock					06/22/20	018		М	4,361		,361	61 A			8,061			D	
Common Stock					06/22/20	018		S		4,	361(1)	D	\$65		3,700			D	
				Table I							d of, or Beneficially Owned vertible securities)		ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative cquired (A) o f (D) (Instr. 3,	r Expirat	on Dat			d Amount of Se Security (Instr		nderlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title			Amount or Number of Shares		Following Reported Transaction(s (Instr. 4)			
Stock Option (Right to Buy)	\$2.9	06/22/2018		M			4,361	(2)		04/27/2020	+		4	,361	\$0.00	19,6	39	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-Fact

** Signature of Reporting Person

06/26/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reportion Schoeneck James A	ng Person [*]				2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]										iship of Reporting P applicable) Director	erson(s) t	to Issuer	10% Own	or
(Last)	(First)	(M	iddle)		3. Date of 07/03/20	FEarliest Tra	nsaction (Mo	nth/Day/Ye	ar)					X	Officer (give title	below)			ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, Date	e of Original	Filed (Mon	th/Day	/Year)				6. Individu X	al or Joint/Group F Form filed by Or Form filed by Mo	ne Reporti	ting Pers	on	
(Street) SAN FRANCISCO	CA	94	158																
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	f, or Bene	eficially Ov	wned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	eemed ution Date,	3. Transact Code (Inst		4. Securi		d (A) or Dispo	sed Of (· [5. Amount of Securities Beneficially Owned Following Reported			rship Form: D) or Indirect . 4)	7. Nature of Indirect Beneficial
					(Month/Day		th/Day/Year)	Code	v	Amount		(A) or (D)	Price	1	Fransaction(s) (Instr. I)		(i) (instr	. 4)	Ownership (Instr. 4)
Common Stock					07/03/2	018		М		7	,639	A	\$	2.9	11,339			D	
Common Stock					07/03/2	018		S		7,0	639(1)	D	\$	65	3,700			D	
				Table I		itive Secu outs, calls						cially Owr ies)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative cquired (A) o f (D) (Instr. 3,	r Expirati	on Dat			d Amount of So Security (Instr			8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	ive ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title			unt or ber of es	per of		ing ed ction(s)		
Stock Option (Right to Buy)	\$2.9	07/03/2018		M			7,639	(2)		04/27/2020	Common Stock			7,639	\$0.00		000	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-Fact

** Signature of Reporting Person

07/06/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Schoeneck James A	ing Person [*]				2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]										hip of Reporting Popplicable) Director	erson(s) to	o Issuer	10% Own	or.
(Last)	(First)	(M	iddle)		3. Date of 01/07/20		nsaction (Mo	nth/Day/Yea	ar)					X	Officer (give title	below)			ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Amei	ndment, Date	e of Original	Filed (Mont	th/Day/	/Year)			6. In	dividual X	I or Joint/Group F Form filed by On Form filed by Mo	e Reporti	ing Perso	on ,	
(Street) SAN FRANCISCO	CA	94	158												,		•	3	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	curities A	cquired,	Disp	osed of	f, or Bene	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exec	eemed ution Date,	3. Transact Code (Instr		4. Securi		ed (A) or Dispo	sed Of (D)	Be	5. Amount of Securities Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(Month/Day		th/Day/Year)	Code	v	Amount		(A) or (D)	Price		ansaction(s) (Instr.		(i) (instr.	4)	Ownership (Instr. 4)
Common Stock					01/07/20	019		М		2	2,000	A	\$2.9		29,700			D	
Common Stock					01/07/20	019		S		2,0	000(1)	D	\$45.9		27,700			D	
				Table I			rities Acc					icially Owr	ied						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities A	of Derivative cquired (A) o f (D) (Instr. 3,		on Dat			d Amount of So Security (Instr		erlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	/e I	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)	Date Exercisa		Expiration Date	Title		Amount of Number of Shares			Followir Reported Transact (Instr. 4)	d tion(s)		, , , , , , , , , , , , , , , , , , ,
Stock Option (Right to Buy)	\$2.9	01/07/2019		M			2,000	(2)		04/27/2020	Common Stock		2,0	00	\$0.00		00	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-Fact

** Signature of Reporting Person

01/09/2019

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

ı	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporti Schoeneck James A	1. Name and Address of Reporting Person Schoeneck James A						cker or Tradi	0 ,						ship of Reporting Pe applicable) Director	erson(s) to	o Issuer	10% Own	er	
(Last)	(First)	(M	iddle)		3. Date of Earliest Transaction (Month/Day/Year) 02/07/2019										Officer (give title	below)		Other (specify below)	
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	If Amendment, Date of Original Filed (Month/Day/Year)									vidual or Joint/Group Filing (Check Applicable Line) Form filed by One Reporting Person Form filed by More than One Reporting Person				
(Street) SAN FRANCISCO	CA												•		·	Ü			
(City)																			
Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned																			
1. Title of Security (Instr. 3)					2. Transaction 2A. Deemed Execution Date (Month/Day/Year) if any		ution Date,	3. Transaction 4. Securit (Instr. 3,		rities Acquired (A) or Disposed Of , 4 and 5)		sed Of (E	́ в	Amount of Securiti eneficially Owned ollowing Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial	
					(MONTH/Day		th/Day/Year)	Code V	ode V Amount			(A) or (D)	Price	T	Transaction(s) (Instr. 3 and 4)		(1) (111341. 4)		Ownership (Instr. 4)
Common Stock					02/07/2019		М		2,	2,000 A		\$2	2.9	29,700		D			
Common Stock					02/07/20	019		S		2,0	000(1)	D	\$57	7.17	27,700			D	
				Table I		itive Secu outs, calls						cially Own ies)	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code		of Derivative cquired (A) o (D) (Instr. 3,		n Date			I Amount of Se Security (Instr			8. Price of Derivative Security (Instr. 5)	9. Number derivative Securitie Beneficia	re F	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code			Date Exercisab		xpiration ate	N N			unt or ber of es		Followin Reported Transacti (Instr. 4)	d tion(s)		(*)	
Stock Option (Right to Buy)	\$2.9	02/07/2019		M			(2)	0	4/27/2020	Common Stock			2,000	\$0.00		00	D		

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-Fact

** Signature of Reporting Person

02/08/2019

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $^{^{\}star}$ If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep Schoeneck James A	1. Name and Address of Reporting Person* Schoeneck James A							ng Symbol					ionship of Reporting F all applicable) Director	Person(s) to		6 Owner	
(Last)	(First)	(M	iddle)		3. Date of 03/07/20		nsaction (Mo	nth/Day/Year				Officer (give title	e below)		er (specify below)		
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Amer	ndment, Date	e of Original	Filed (Month/	Day/Year)			Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person					
(Street) SAN FRANCISCO	CA	94	158										·				
(City)	(State)	(Zi	p)														
			T	able I -	Non-Deri	vative Se	curities A	.cquired, [isposed	l of, or Ben	neficially Ow	ned					
1. Title of Security (Instr. 3)				Date			3. Transaction Code (Instr. 8		curities Acquir . 3, 4 and 5)	ed (A) or Dispos	ed Of (D)	5. Amount of Securi Beneficially Owned Following Reported		6. Ownership For Direct (D) or Indi (I) (Instr. 4)			
					(Month/Day/			Code	Amou	Amount (A) or (D)		Price	Transaction(s) (Instr		(1) (1110111 1)	Ownership (Instr.	
Common Stock					03/07/2019		М		2,000	A	\$2.9	29,700		D			
Common Stock					03/07/2019			S		1,620(1)	D	\$54.62 ⁽²⁾	28,080		D		
Common Stock					03/07/2019		S	380 ⁽¹⁾ D \$5			\$55.23 ⁽³⁾	27,700		D			
				Table I				•	•	f, or Benef tible securi	ficially Own ities)	ed					
				4. Transa (Instr. 8)	ction Code	5. Number of Securities A Disposed of 4 and 5)	cquired (A) o	r Expiration			nd Amount of Se e Security (Instr.		8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Beneficia Owned	re Form: Di es (D) or Inc	rect Indirect lirect Beneficial	
	Security Code V (A) (D) Exercisable Expiration Date Title						Amount or Number of Shares		Followin Reported Transact (Instr. 4)	d tion(s)							
Stock Option (Right to Buy)	\$2.9	03/07/2019		M			2,000	(4)	04/27/20	20 Common Stock		2,000	\$0.00	6,00	00 D		

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$54.05 to \$55.04. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$55.05 to \$55.38. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Fully vested.

Remarks:

03/08/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Schoeneck James A	1. Name and Address of Reporting Person* Schoeneck James A							ng Symbol					(Chec	k all ap	ip of Reporting Peoplicable) Director	erson(s)	to Issuer	10% Own	or.
(Last)	(First)	(M	iddle)		3. Date of 04/08/20		ansaction (Mo	nth/Day/Ye	ar)						Officer (give title	below)			ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Amer	ndment, Da	te of Original	th/Day/	/Year)		- 1	dividual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person							
(Street) SAN FRANCISCO	CA	94	158												,		•	J	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative Se	ecurities A	cquired	, Disp	osed of	f, or Bene	eficially Ov	wned						
1. Title of Security (Instr. 3)							3. Transaction Code (Instr. 8) 4. Securities Acquired (A) or Dispo			ed (A) or Dispo	sed Of (D)	Ber	5. Amount of Securities Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial		
					(MOIIII/Day		nth/Day/Year)	Code	de V Amoun			(A) or (D)	Price		Transaction(s) (Instr. 3 and		(., (51. 7)		Ownership (Instr. 4)
Common Stock					04/08/20)19		M		2	2,000	A	\$2.9		29,700			D	
Common Stock					04/08/20	019		S		2,	000(1)	D	\$52.9 ⁽²⁾		27,700			D	
				Table I			urities Acc s, warrant					icially Owr	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)			Exercis ion Date Day/Yea			d Amount of So Security (Instr	ecurities Under : 3 and 4)	rlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic Owned	ive ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		FoII Rep		ing ed ction(s)		4)
Stock Option (Right to Buy)	\$2.9	04/08/2019		M			2,000	(3)		04/27/2020	Com	Common Stock		2,000 \$0.00		4,000		D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$52.69 to \$53.27. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. Fully vested.

Remarks:

/s/ Michael Lowenstein, Attorney-in-Fact

04/10/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	Name and Address of Reporting Person* Schoeneck James A						Ticker or Trac VC [FGEN	0 ,	mbol				(Check	Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director 10% Owner					ner
(Last)	(First)	(M	iddle)		3. Date of 05/07/20		ransaction (M	onth/Day	y/Year)					Officer (give title below) Other (spec					
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	l Filed ((Month/Da	y/Year)		Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person							
(Street) SAN FRANCISCO	CA	94	158												,			J	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	vative S	ecurities A	Acquir	red, Dis	posed o	f, or Ber	neficially Ov	vned						
1. Title of Security (Instr. 3)					Date		2A. Deemed Execution Date, r) if any				4. Securities Acquired (A) or Disposed Of (Instr. 3, 4 and 5)			Ben	5. Amount of Securities Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(MOIIII/Day		(Month/Day/Year)		v	Amount		(A) or (D)	Price		nsaction(s) (Instr.	3 and	,,,,,,		Ownership (Instr. 4)
Common Stock					05/07/2019		M		1	2,000	A	\$2.9		5,700			D		
Common Stock					05/07/2019					1,	500(1)	D	\$46.8 ⁽²⁾	4,200		10		D	
Common Stock					05/07/2019			S		5	500(1)	D	\$47.69 ⁽³⁾	3,700				D	
Common Stock															24,000			I	By trust
				Table I			curities Ac					ficially Own	ed						
nstr. 3) Conversion or Exercise Price of Price O					ction Code	Securities	r of Derivative Acquired (A) of (D) (Instr. 3	or Exp	Date Exerc piration Da onth/Day/Yo			nd Amount of Se e Security (Instr		lying	Derivative derivative Security (Instr. 5) Derivative derivative Security (Instr. Benefi		rities (D) or Indire		11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Derivative Security			Amount or Number of Shares	F R T		Owned Following Reported Transaction(s) (Instr. 4)		1										
Stock Option (Right to Buy)	\$2.9	05/07/2019		M			2,000		(4)	04/27/2020	Co	mmon Stock	2,000)	\$0.00	2,0	000	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$46.16 to \$47.14. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$47.27 to \$48.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-Fact

05/09/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Schoeneck James A	. Name and Address of Reporting Person* Schoeneck James A						cker or Tradi	I			5. Relation (Check a	ll applic	of Reporting Pe cable) ector	erson(s) t	to Issuer	10% Own	er		
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date o 01/06/20		nsaction (Mo	nth/Day/Ye	ear)				X	X Officer (give title below) Other (specify bel Interim President					
409 ILLINOIS ST.					4. If Ame	ndment, Dat	e of Original	nth/Day	/Year)		6. Individ	6. Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person							
	CA (State)											For	rm filed by Mo	re than (One Repo	orting Person			
(City)																			
			l	able I -				•	•	_	•	ficially Ov							
1. Title of Security (Instr. 3)					Date Execution Date, (Month/Day/Year) if any		3. Transaction Code (Instr. 8) 4. Securities Acquired (A) or Disposed C (Instr. 3, 4 and 5)			` '	Beneficially Own			d Direct (D) or		7. Nature of Indirect			
							Code	v	Amount	Amount (A) or (D)		Price	Following Reported Transaction(s) (Inst 4)				. 4)	Beneficial Ownership (Instr. 4)	
Common Stock					01/06/2	020		F		10,	928(1)	D	\$43.35		22,422(2)			D	
				Table I			irities Acc s, warrants	•				cially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)					ction Code	Securities A	of Derivative Acquired (A) o f (D) (Instr. 3,	r Expirat	tion Dat		7. Title and Amount of Securiti Derivative Security (Instr. 3 and			ng 8. Price of Derivative Security (Instr		9. Number of derivative Securities Beneficially		10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
			Code	v	(A)	(D)	Date Exercis	Date Expi Exercisable Date		ration Nun		Amount or Number of Shares		Foll Rep Trai		wned ollowing eported ransaction(s) nstr. 4)		4)	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Reflects the cancellation on January 6, 2020 of 28,650 shares pursuant to the vesting terms of the RSU grant.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

01/08/2020

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

EXHIBIT EEE

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Ch	neck this box if no longer subject to Section 16. Forn
4 (or Form 5 obligations may continue. See Instruction
1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden
hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]		2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)										k all ap	p of Reporting Pe plicable) Director	erson(s) t	to Issuer	10% Own	er		
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 05/19/20		st Transaction (Month	n/Day/Yea	ar)						Officer (give title		cutive Of	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	t, Date of Origir	nal Fil	led (Mont	th/Day/	/Year)					or Joint/Group Fi Form filed by On			,	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	re than C	One Repo	ting Person	
(City)	(State)	(Zi	p)																	
			Т	able I - I	Non-Deri	vativ	e Securities	Acc	quired,	Disp	osed of	, or Ben	eficially Ov	ned						
1. Title of Security (Instr. 3)					2. Transact Date		2A. Deemed Execution Date	3. Co	Transacti de (Instr		4. Securit (Instr. 3, 4		d (A) or Dispos	ed Of (D)	Ben	mount of Securiti eficially Owned		Direct (D)	ship Form: or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day/Yea	r) c	ode	v	Amount		(A) or (D)	Price		owing Reported isaction(s) (Instr.		(I) (Instr.	1)	Beneficial Ownership (Instr. 4)
Common Stock					05/19/20	016			S		12,8	800(1)	D	\$17.45 ⁽²⁾		3,526,053			D	
Common Stock					05/19/20	016			S		70	00(1)	D	\$18.12 ⁽³⁾		3,525,353			D	
Common Stock					05/20/20	016			S		13,5	500(1)	D	\$17.88(4)		3,511,853			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁵⁾
				Table I			Securities A calls, warra							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	4. Transa (Instr. 8)	nsaction Code 5. N 8) Sec		. Number of Derivative curities Acquired (Aisposed of (D) (Instrand 5)		6. Date E Expiration (Month/E	on Dat	e		d Amount of Se Security (Instr.		rlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici	ve F	0. Ownership orm: Direct D) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.	
	Derivative Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Owned Followin Reporte Transact (Instr. 4)	ed tion(s)		4)

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan
- 2. The shares were sold at prices ranging from \$17.17 to \$17.93. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$18.01 to \$18.26. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

- 4. The shares were sold at prices ranging from \$17.30 to \$18.07. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Melissa Leon, Attorney-in-Fact

05/20/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

ı	Check this box if no longer subject to Section 16. Form
	4 or Form 5 obligations may continue. See Instruction
	1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden
hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]			2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)										all ap	o of Reporting Pe blicable) Director	erson(s) t	to Issuer	10% Own	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/01/20		st Transaction (I	Month	/Day/Yea	ar)				X		Officer (give title		cutive Of	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	t, Date of Origin	al Fil	ed (Mont	h/Day/	(Year)			6. Indiv		or Joint/Group F				
(Street) SAN FRANCISCO	CA	94	158												F	orm filed by Mo	re than C	One Repor	ting Person	
(City)	(State)	(Zi	p)																	
			Т	able I - I	Non-Deri	vativ	e Securities	Acq	uired,	Disp	osed of	, or Ben	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transacti Date		2A. Deemed Execution Date,	3. Co	Transaction de (Instr.		4. Securit (Instr. 3, 4		d (A) or Dispos	ed Of (D)	Bene	nount of Securiti		Direct (D)	ship Form: or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day/Year) c.	de \	v	Amount		(A) or (D)	Price		owing Reported saction(s) (Instr.		(I) (Instr.	1)	Beneficial Ownership (Instr. 4)
Common Stock					06/01/20	016		Τ	F		4,6	89(1)	D	\$18.89		3,507,164			D	
Common Stock					06/02/20)16			S		13,5	500(2)	D	\$19 .16 ⁽³⁾		3,493,664			D	
Common Stock					06/03/20	016			S		13,5	500(2)	D	\$ 18.81 ⁽⁴⁾		3,480,164			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁵⁾
				Table I			Securities A calls, warra							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	nsaction Code 5. I		mber of Derivativ ities Acquired (A sed of (D) (Instr. 5)	or	6. Date E Expiration (Month/D	on Date	e		d Amount of Se Security (Instr.		ying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici	ve F es (1	0. Ownership orm: Direct D) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Owned Followin Reporte Transact (Instr. 4)	tion(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Shares sold pursuant to a 10b5-1 plan.
- 3. The shares were sold at prices ranging from \$18.62 to \$19.46. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

- 4. The shares were sold at prices ranging from \$18.25 to \$19.09. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/03/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Ch	neck this box if no longer subject to Section 16. Forn
4 (or Form 5 obligations may continue. See Instruction
1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden
hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo							nd Ticker or Tra	•	Symbol						onship of Re all applicabl Directo	,	erson(s) to	o Issuer	10% Own	or	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/14/20		t Transaction (I	Month/	Day/Year))					X		(give title I		cutive Of	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	, Date of Origin	al File	ed (Month/l	Day/Y	'ear)				6. Individ		nt/Group Fil filed by One			•	
(Street) SAN FRANCISCO	CA	94	158													Form f	filed by Mor	e than Oi	ne Repor	ting Person	
(City)	(State)	(Zi	p)																		
			Т	able I -	Non-Deri	ivative	Securities	Acq	uired, D	Dispo	osed of	, or Bene	eficially Ov	vned							
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		2A. Deemed Execution Date, if any		ransaction de (Instr. 8)		4. Securit (Instr. 3, 4		d (A) or Dispos	ed Of (D)	5. Amount Beneficiall Following		[hip Form: or Indirect	7. Nature of Indirect Beneficial
					(Wonth/Day		ir any (Month/Day/Year	Cod	de V		Amount		(A) or (D)	Price			n(s) (Instr. 3		(I) (INSTr. 4	•)	Ownership (Instr. 4)
Common Stock					06/14/20	016			S		13,5	500(1)	D	\$16	5.47(2)	3	,466,664			D	
Common Stock					06/15/20	016			S		13,5	500(1)	D	\$16	5.49(3)	3	,453,164			D	
Common Stock																1	145,070			I	By Family Partnership
Common Stock																	20,000			I	By Spouse
Common Stock																	60,946			I	See footnote ⁽⁴⁾
				Table I			Securities A calls, warrai	•		•	-		•	ed							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securit	nber of Derivativ ties Acquired (A sed of (D) (Instr. 5)	or I	6. Date Exe Expiration (Month/Day	Date			d Amount of Se Security (Instr			Deriv	vative irity (Instr.	9. Numbe derivative Securities Beneficia	e F	0. Ownership orm: Direct D) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisabl		xpiration ate	Title			ount or nber of res			Owned Followin Reported Transacti (Instr. 4)	d ion(s)		4)

Explanation of Responses:

- 1 Shares sold pursuant to a 10b5-1 plan
- 2. The shares were sold at prices ranging from \$16.21 to \$17.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$16.05 to \$16.74. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Melissa Navarro, Attorney-in-fact

06/16/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Check this box if no longer subject to Section 16. Forr
4 or Form 5 obligations may continue. See Instruction
1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287

Expires: December 31, 2014

Estimated average burden
hours per response: 0.5

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Neff Thomas B	ting Person [*]			2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)										all app	of Reporting Pelicable)	erson(s) t	to Issuer	10% Owr	ner	
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/28/20		st Transaction (I	Month	n/Day/Yea	ar)				X		fficer (give title		cutive Of	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	t, Date of Origin	al File	ed (Mont	th/Day/	Year)			6. Indiv		r Joint/Group Fi orm filed by On				
(Street) SAN FRANCISCO	CA	94	158												F	orm filed by Mo	re than C	One Repor	ting Person	
(City)	(State)	(Zi	p)																	
			Т	able I - I	Non-Deri	vative	e Securities	Acc	quired,	Disp	osed of	, or Ben	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transacti Date		2A. Deemed Execution Date,	3. Co	Transacti de (Instr.		4. Securit (Instr. 3, 4		d (A) or Dispos	ed Of (D)	Bene	nount of Securiti		Direct (D)	hip Form: or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day/Year) c _°	ode	v	Amount		(A) or (D)	Price		wing Reported action(s) (Instr.		(I) (Instr. 4	1)	Beneficial Ownership (Instr. 4)
Common Stock					06/28/20	016		Τ	S		13,4	400(1)	D	\$15.87(2)		3,439,764			D	
Common Stock				ĺ	06/28/20	016			S		10	00(1)	D	\$16.21		3,439,664			D	
Common Stock					06/29/20	016			S		13,5	500(1)	D	\$16.17 ⁽³⁾		3,426,164			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table I			Securities A calls, warra							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securi	mber of Derivativ ities Acquired (A sed of (D) (Instr. 5)	or	6. Date E Expiration (Month/E	on Date	e		d Amount of Se Security (Instr.			8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici	ve F es (I	0. Ownership orm: Direct 0) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Owned Followin Reporte Transact (Instr. 4)	tion(s)		4)

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan
- 2. The shares were sold at prices ranging from \$15.20 to \$16.19. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$15.95 to \$16.38. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/30/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep Neff Thomas B	orting Person*						Ticker or Trac		Symbol					tionship of Reportir all applicable) Director	g Person(s		r X 10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 07/12/20		ransaction (M	¶onth/[Day/Year)				X		chief Ex	1	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	al Filed	d (Month/Da	ay/Year)			6. Indiv	ridual or Joint/Grou			•	
(Street) SAN FRANCISCO	CA	94	158											Form filed by	More than	One Rep	porting Person	
(City)	(State)	(Zi	p)															
			Т	able I - I	Non-Deri	vative S	Securities .	Acqı	uired, Dis	sposed	of, or Ben	eficially Ov	ned					
1. Title of Security (Instr. 3)					2. Transacti Date	Exe	. Deemed ecution Date,		ransaction le (Instr. 8)		rities Acquire 3, 4 and 5)	ed (A) or Dispos	ed Of (D)	5. Amount of Sec Beneficially Own	ed	Direct (ership Form: (D) or Indirect	7. Nature of Indirect
					(Month/Day		iny onth/Day/Year)	Cod	le V	Amoun	t	(A) or (D)	Price	Following Repor Transaction(s) (Ir 4)		(I) (Insti	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					07/12/20	016			S	1	3,500(1)	D	\$17.81(2)	3,412,6	64		D	
Common Stock					07/13/20)16			S	2	2,700(1)	D	\$16.96(3)	3,409,9	64		D	
Common Stock					07/13/20)16			S	1	0,800(1)	D	\$17.24 ⁽⁴⁾	3,399,1	64		D	
Common Stock														145,07	0		I	By Family Partnership
Common Stock														20,00)		I	By Spouse
Common Stock														60,94	5		I	See footnote ⁽⁵⁾
				Table I			curities Ad Ils, warran					icially Own ties)	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	er of Derivative s Acquired (A) d of (D) (Instr. :	or E	6. Date Exerc Expiration D Month/Day/Y	ate		d Amount of Se Security (Instr.		ying 8. Price of Derivative Security (In 5)	deriva	ities icially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercisable	Expiratio Date	n Title		Amount or Number of Shares		Follow Repor	ving ted action(s)		* ')

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan
- 2. The shares were sold at prices ranging from \$17.29 to \$18.03. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$16.87 to \$16.995. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

- 4. The shares were sold at prices ranging from \$17.00 to \$17.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/14/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	ast) (First) (Middle) /O FIBROGEN, INC.						icker or Trac	-	symbol					(Chec	k all ap	p of Reporting Pe plicable) Director	erson(s) to		【 10% Owr	or
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 07/26/20		ansaction (M	onth/E	Day/Year)							Officer (give title	below)		Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	te of Origina	l Filed	d (Month/D	ay/Year)						or Joint/Group Fi			•	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo		-		
(City)	(State)	(Zi	p)																	
			Т	able I - I	Non-Deri	vative S	ecurities A	Acqu	uired, Di	sposed	of, or I	Benef	icially Ov	ned						
1. Title of Security (Instr. 3)					2. Transact Date	Exe	Deemed cution Date,		ansaction e (Instr. 8)		curities Ac		(A) or Dispos	ed Of (D)	Ben	mount of Securiti		Direct (I	ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		y ith/Day/Year)	Code	e V	Amou	ınt	(A) or (D)	Price		owing Reported saction(s) (Instr.		(I) (Instr	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					07/26/20	016		N	М		14,091		Α	\$4.025		3,413,255			D	
Common Stock					07/26/20	016		5	S		14,799(1)		D	\$18.28 ⁽²⁾		3,398,456			D	
Common Stock					07/26/20	016		5	S		4,100(1)		D	\$ 18.57 ⁽³⁾		3,394,356			D	
Common Stock					07/27/20	016		N	М		14,091		A	\$4.025		3,408,447			D	
Common Stock					07/27/20	016		5	S		18,899(1)		D	\$18.4076 ⁽⁴		3,389,548			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁵⁾
				Table I			urities Ac s, warran							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) of (D) (Instr. 3	or E	5. Date Exer Expiration D Month/Day/	Date			Amount of Se ecurity (Instr.	curities Unde 3 and 4)	rlying	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securitie Beneficia	e s	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisable	Expirat Date	ion Title			Amount or Number of Shares			Owned Followin Reported Transacti (Instr. 4)	ĭ		4)

				Table II			•			or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	tion Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	07/26/2016		M			14,091	(6)	02/28/2017	Common Stock	14,091	\$0.00	295,909	D	
Stock Option (Right to Buy)	\$4.025	07/27/2016		M			14,091	(6)	02/28/2017	Common Stock	14,091	\$0.00	281,818	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$17.55 to \$18.54. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$18.55 to \$18.61. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$18.16 to \$18.71. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 6. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/28/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
l	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	orting Person*						icker or Trac C [FGEN	-	symbol						onship of Reporting F Ill applicable) Director	Person(s) t		10% Owr	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 08/25/20		ansaction (M	onth/[Day/Year)					X	Officer (give title	e below) Chief Exec		Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, Da	te of Origina	l Filed	d (Month/Da	ay/Year)				6. Individ	lual or Joint/Group I Form filed by O			•	
(Street) SAN FRANCISCO	CA	94	158											A	Form filed by M	•	•		
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Deri	vative S	curities A	Acqı	uired, Di	sposed	of, or Be	neficially (Owne	d					
1. Title of Security (Instr. 3)					2. Transact Date	Exe	eemed ution Date,		ansaction e (Instr. 8)		urities Acqu 3, 4 and 5)	ired (A) or Disp	osed O	f (D)	5. Amount of Securit Beneficially Owned		Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		y th/Day/Year)	Cod	e V	Amour	nt	(A) or (D)	Price	•	Following Reported Transaction(s) (Instr 4)		(I) (Insti	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					08/25/20	016		N	М		14,091	A		\$4.025	3,403,639			D	
Common Stock					08/25/20	016			S	1	7,699(1)	D	\$	17.76 ⁽²⁾	3,385,940			D	
Common Stock					08/25/20	016			S		1,200(1)	D	\$	18.15(3)	3,384,740			D	
Common Stock					08/26/20	016		N	M		14,091	A	,	4.025	3,398,831			D	
Common Stock					08/26/20	016			S	1	8,899(1)	D	\$	17.81 ⁽⁴⁾	3,379,932			D	
Common Stock															145,070			I	By Family Partnership
Common Stock															20,000			I	By Spouse
Common Stock															60,946			I	See footnote ⁽⁵⁾
				Table I			urities Ac s, warran					eficially Ov rities)	vned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securities	of Derivative Acquired (A) of (D) (Instr. 3	or E	5. Date Exer Expiration D Month/Day/	ate		and Amount of ve Security (In			8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisable	Expiration Date	on Title		N N	mount or umber of hares		Owned Followin Reporte Transact (Instr. 4)	tion(s)		4)

				Table II			•			or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)		5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	08/25/2016		M			14,091	(6)	02/28/2017	Common Stock	14,091	\$0.00	267,727	D	
Stock Option (Right to Buy)	\$4.025	08/26/2016		M			14,091	(6)	02/28/2017	Common Stock	14,091	\$0.00	253,636	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$17.13 to \$18.12. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$18.13 to \$18.19. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$17.51 to \$18.11. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 6. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/29/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]						d Ticker or Tra		ymbol						nip of Reporting Popplicable) Director	erson(s) to	lssuer X	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 09/01/20		Transaction (N	Ionth/D	ay/Year)					X	Officer (give title	below) hief Exec	utive O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Origina	al Filed	I (Month/Da	//Year)			6. 1		or Joint/Group F Form filed by On	٠,		,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than O	ne Repo	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Der	ivative	Securities	Acqu	ired, Dis	posed o	f, or Ben	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact Date	E	A. Deemed xecution Date,		ansaction e (Instr. 8)		ities Acquire 4 and 5)	ed (A) or Dispose	ed Of (D)	Be	Amount of Securiti neficially Owned	- 1	Direct (D	ship Form:) or Indirect	7. Nature of Indirect
					(Month/Day		any Month/Day/Year)	Code	e V	Amount		(A) or (D)	Price		llowing Reported insaction(s) (Instr.		(I) (Instr.	4)	Beneficial Ownership (Instr. 4)
Common Stock					09/01/2	016		F	F	4,0	688(1)	D	\$17.3	3	3,375,244			D	
Common Stock															145,070			I	By Family Partnership
Common Stock															20,000			I	By Spouse
Common Stock															60,946			I	See footnote ⁽²⁾
				Table I			ecurities Ad alls, warran	•				icially Owne	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securiti	per of Derivative es Acquired (A) ed of (D) (Instr.)	or Ex	. Date Exerc xpiration Da Month/Day/Ye	te		d Amount of Sec Security (Instr.		derlying	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securitie Beneficia	e l	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		ate xercisable	Expiration Date	Title		Amount Number Shares			Owned Followin Reported Transacti (Instr. 4)	ľ		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/02/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B (Last) C/O FIBROGEN, INC.	rting Person* (First)	(M	iddle)		3. Date o 09/08/20	OGEN f Earlies 16	INC FGE	N] (Mont	th/Day/Y	ear)				(Checl	k all ap		below) nief Exec	X cutive C	(10% Own Other (sp	er ecify below)
409 ILLINOIS ST. (Street) SAN FRANCISCO (City)	CA (State)	94 (Zi					, Date of Origi							2	K I	or Joint/Group F Form filed by On Form filed by Mo	e Reportii	ng Pers	on	
4 774 - 40 40 - 40 - 40 - 0			Т	able I -	Non-Deri		Securities 2A. Deemed	_	quired		_		eficially Ov		1	mount of Securiti	[.		ership Form:	7. Nature of
1. Title of Security (Instr. 3)					Date (Month/Day	/Year) i	ZA. Deemed Execution Date if any (Month/Day/Yea	, c	ode (Ins		(Instr. 3,		(A) or Dispos	Price	Ben Foll	eficially Owned owing Reported esaction(s) (Instr.			D) or Indirect	Indirect Beneficial Ownership (Instr. 4)
Common Stock					09/08/20	016			M		14	1,091	A	\$4.025	T	3,389,335			D	
Common Stock					09/08/20	016			S		18,	899(1)	D	\$19.14 ⁽²⁾	\top	3,370,436			D	
Common Stock					09/09/20	016			M		14	1,091	A	\$4.025		3,384,527			D	
Common Stock					09/09/20	016		Ť	S		18,	899(1)	D	\$18.83 ⁽³⁾		3,365,628			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table I			Securities A						icially Own ties)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ection Code	Securit	nber of Derivati ties Acquired (sed of (D) (Inst	A) or	Expira	Exerci tion Da n/Day/Ye			d Amount of Se Security (Instr.		lying	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securitie Beneficia Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercis	sable	Expiration Date	Title		Amount or Number of Shares			Followin Reported Transacti (Instr. 4)	d tion(s)		
Stock Option (Right to Buy)	\$4.025	09/08/2016		М			14,0	91	(5)	02/28/2017	Con	nmon Stock	14,09	1	\$0.00	239,5	545	D	
				1	1	1	1		1			1								1

				Table II			•	, .	•	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	(Instr. 3) Conversion or Exercise Price of Price														
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	09/09/2016		M			14,091	(5)	02/28/2017	Common Stock	14,091	\$0.00	225,454	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$18.80 to \$19.32. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$18.31 to \$19.11. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/09/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B	rting Person*	(M	iddle)		FIBRO	OGEN f Earlies	nd Ticker or Ti INC [FGE st Transaction	N]						(Chec	k all ap X	ip of Reporting P plicable) Director Officer (give title		y	10% Owr	er ecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST.					4. If Ame	ndment,	, Date of Origi	nal F	iled (Mo	nth/Day	//Year)					or Joint/Group F Form filed by On	•		*	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo		-		
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Der	ivative	Securities	s Ac	quired	d, Dis	posed o	f, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact		2A. Deemed Execution Date if any		Transac		4. Securi (Instr. 3,		ed (A) or Dispos	sed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	.	Direct (I	ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		(Month/Day/Yea	r) c	ode	v	Amount		(A) or (D)	Price		nsaction(s) (Instr.		(I) (Instr	. 4)	Ownership (Instr. 4)
Common Stock					09/20/20	016			M		14	1,091	A	\$4.025		3,379,719			D	
Common Stock					09/20/20	016			S		18,	899(1)	D	\$21.8 ⁽²⁾		3,360,820			D	
Common Stock					09/21/20	016			M		14	1,091	A	\$4.025		3,374,911			D	
Common Stock					09/21/20	016			S		18,	899(1)	D	\$21.52(3)		3,356,012			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table			Securities A						ficially Own	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	iction Code	Securit	nber of Derivati ties Acquired (a sed of (D) (Insti	A) or	Expira	e Exerci ition Da n/Day/Ye			nd Amount of Se Security (Instr		rlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercis	sable	Expiration Date	Title		Amount or Number of Shares			Following Reporte Transact (Instr. 4)	d tion(s)		4)
Stock Option (Right to Buy)	\$4.025	09/20/2016		М			14,0	91	(5)	02/28/2017	Cor	nmon Stock	14,0	01	\$0.00	211,3	363	D	
				1	1	1	1		1											

				Table II			•	, .	,	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	09/21/2016		M			14,091	(5)	02/28/2017	Common Stock	14,091	\$0.00	197,272	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$21.30 to \$22.16. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$21.02 to \$21.91. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/22/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B (Last) C/O FIBROGEN, INC. 409 ILLINOIS ST.	rting Person* (First)	(M	iddle)		3. Date o 10/03/20	GEN f Earlies 116	nd Ticker or Tr INC [FGE] It Transaction (Mont	h/Day/Ye	ear)	//Year)			(Chec	k all ap	ip of Reporting P plicable) Director Officer (give title C) or Joint/Group F	below) hief Exec	Scutive C	10% Owr Other (sp	er ecify below)
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158 p)			,	, 24.0 0 0 1g.								X	Form filed by On	ie Reporti	ing Pers	on	
			Т	able I -			Securities	_	-						1					
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	/Year) i	2A. Deemed Execution Date if any (Month/Day/Yea	c	Transact		4. Securi (Instr. 3,		(A) or (D)	Price	Ben Foli	mount of Securiti eficially Owned owing Reported nsaction(s) (Instr.			ership Form: D) or Indirect :. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
Common Stock					10/03/20	016			M		14	l,091	A	\$4.025	1	3,370,103			D	
Common Stock					10/03/20	016		T	S		18,	899(1)	D	\$20.55(2)	\top	3,351,204			D	
Common Stock					10/04/20	016			M		14	,091	A	\$4.025		3,365,295			D	
Common Stock					10/04/20	016			S		18,	899(1)	D	\$20.67(3)		3,346,396			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table I			Securities A							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	iction Code	Securit	nber of Derivati ties Acquired (A sed of (D) (Instr 5)) or	6. Date Expirat (Month/	ion Da			d Amount of Se Security (Instr		rlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercis		Expiration Date	Title		Amount or Number of Shares			Followin Reporte Transact (Instr. 4)	d tion(s)		,
Stock Option (Right to Buy)	\$4.025	10/03/2016		М			14,09	91	(5)		02/28/2017	Con	nmon Stock	14,09	91	\$0.00	183,	181	D	

				Table II			•	, .	•	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	10/04/2016		М			14,091	(5)	02/28/2017	Common Stock	14,091	\$0.00	169,090	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$20.16 to \$20.86. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$20.35 to \$20.99. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

10/05/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B					FIBRO	OGEN f Earlies	nd Ticker or Tr <u>INC</u> [FGEN st Transaction (1]							all ap	p of Reporting Policable) Director Officer (give title		o Issuer	√ 10% Owr	er ecify below)
(Last) C/O FIBROGEN, INC. 409 ILLINOIS ST.	(First)	(M	iddle)				, Date of Origii	nal Fi	led (Mor	nth/Day	//Year)			6. Indiv		or Joint/Group F		eck Appl	licable Line)	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	-	-		
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Der	ivative	Securities	Ac	quired	l, Dis	posed of	f, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		2A. Deemed Execution Date if any		Transac ode (Inst		4. Securi (Instr. 3,		ed (A) or Dispos	ed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	.		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month Day		(Month/Day/Yea	r) c	ode	v	Amount		(A) or (D)	Price		saction(s) (Instr.		(1) (111341	1	Ownership (Instr. 4)
Common Stock					10/18/20	016			M		14	,091	A	\$4.025		3,360,487			D	
Common Stock					10/18/20	016			S		18,	899(1)	D	\$17.94 ⁽²⁾		3,341,588			D	
Common Stock					10/19/20	016			M		14	,091	A	\$4.025		3,355,679			D	
Common Stock					10/19/20	016			S		18,	899(1)	D	\$17.56 ⁽³⁾		3,336,780			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table I			Securities A calls, warra							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securi	nber of Derivati ties Acquired (A sed of (D) (Instr 5)) or	Expirat				d Amount of Se Security (Instr		lying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercis	sable	Expiration Date	Title		Amount or Number of Shares			Followin Reporte Transact (Instr. 4)	d tion(s)		4)
Stock Option (Right to Buy)	\$4.025	10/18/2016		М			14,09	91	(5))	02/28/2017	Con	nmon Stock	14,091	1	\$0.00	154,9	999	D	
					1	1	1	_	_	7				1						

Case 3:21-cv-02623-EMC Document 111 Filed 01/14/22 Page 1572 of 1730

				Table II			•	, .	•	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	10/19/2016		М			14,091	(5)	02/28/2017	Common Stock	14,091	\$0.00	140,908	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$17.75 to \$18.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$17.35 to \$17.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

10/19/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B (Last) C/O FIBROGEN, INC. 409 ILLINOIS ST.	rting Person* (First)	(M	iddle)		3. Date o 10/31/20	GEN f Earlies 116	INC [FGEN st Transaction (I	Month	n/Day/Yea		//Year)			(Chec	k all ap	ip of Reporting P plicable) Director Officer (give title Cl or Joint/Group F	below) hief Exec	Scutive C	10% Own Other (sp	er ecify below)
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	158 p)													Form filed by On	-	-		
			Т	able I -	Non-Deri	ivative	Securities	Acc	quired,	Dis	posed of	f, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	/Year) i	2A. Deemed Execution Date, if any (Month/Day/Year	Co	Transacti ode (Instr		4. Securi (Instr. 3,		(A) or Dispos	ed Of (D)	Ben Foli	mount of Securiti eficially Owned owing Reported nsaction(s) (Instr.			ership Form: D) or Indirect r. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
Common Stock					10/31/20	016			M		14	l,091	A	\$4.025	1"	3,350,871			D	
Common Stock					10/31/20	016			S		18,	899(1)	D	\$16.67(2)		3,331,972			D	
Common Stock					11/01/20	016			M		14	,091	A	\$4.025	\top	3,346,063			D	
Common Stock					11/01/20	016		T	S		18,	899(1)	D	\$16.84 ⁽³⁾		3,327,164			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table I			Securities A							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	iction Code	Securit	nber of Derivativ ities Acquired (A sed of (D) (Instr. 5)) or	6. Date I Expirati (Month/I	on Dat			d Amount of Se Security (Instr		rlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Amount or Number of Shares			Followir Reported Transact (Instr. 4)	d tion(s)		4)
Stock Option (Right to Buy)	\$4.025	10/31/2016		М			14,09	1	(5)		02/28/2017	Con	nmon Stock	14,09	91	\$0.00	126,8	817	D	
								٦										Т		

Case 3:21-cv-02623-EMC Document 111 Filed 01/14/22 Page 1574 of 1730

				Table II			•	, .	,	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	11/01/2016		М			14,091	(5)	02/28/2017	Common Stock	14,091	\$0.00	112,726	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$16.40 to \$17.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$16.55 to \$17.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

11/01/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B	ting Person*						Ticker or Trac		/mbol					all ap	o of Reporting Policable) Director	erson(s) to	Issuer	₹ 10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 11/16/20		ransaction (N	lonth/D	ay/Year)				X		Officer (give title	below)		Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	al Filed	(Month/Da	ıy/Year)			6. Indiv		or Joint/Group Form filed by On			•	
(Street) SAN FRANCISCO	CA	94	1158												Form filed by Mo		-		
(City)	(State)	(Zi	ip)																
			Т	able I -	Non-Deri	ivative S	Securities .	Acqu	ired, Dis	sposed o	f, or Ben	eficially O	vned						
1. Title of Security (Instr. 3)					2. Transact Date	Ex	. Deemed ecution Date,		ansaction (Instr. 8)		ities Acquire 4 and 5)	ed (A) or Dispo	sed Of (D)	Bene	nount of Securiti		Direct (I	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		iny onth/Day/Year)	Code	v	Amount		(A) or (D)	Price		owing Reported saction(s) (Instr.	3 and	l) (Instr	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					11/16/20	016		M	1	1-	4,091	A	\$4.025		3,341,255			D	
Common Stock					11/16/20	016		S		18	,899(1)	D	\$22.36 ⁽²⁾		3,322,356			D	
Common Stock					11/17/20	016		М	1	1-	4,091	A	\$4.025		3,336,447			D	
Common Stock					11/17/20	016		S		18	,899(1)	D	\$22.22(3)		3,317,548			D	
Common Stock															145,070			I	By Family Partnership
Common Stock															20,000			I	By Spouse
Common Stock															60,946			I	See footnote ⁽⁴⁾
				Table I			curities Ac Ils, warran					icially Owr ties)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	iction Code	Securitie	er of Derivative s Acquired (A) d of (D) (Instr.	or Ex	Date Exerc xpiration Day/Y			d Amount of S Security (Inst	ecurities Underl	ying	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securities Beneficia Owned	e s	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		ate xercisable	Expiration Date	Title		Amount or Number of Shares			Following Reported Transaction (Instr. 4)	ĭ		,
Stock Option (Right to Buy)	\$4.025	11/16/2015		М			14,091		(5)	02/28/2017	Con	nmon Stock	14,091		\$0.00	98,63	15	D	
		1											1						

				Table II			•	, .	•	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	11/17/2016		M			14,091	(5)	02/28/2017	Common Stock	14,091	\$0.00	85,544	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$21.80 to \$22.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$21.85 to \$22.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

11/18/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B (Last) C/O FIBROGEN, INC. 409 ILLINOIS ST.	rting Person* (First)	(M	liddle)		2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year) 11/28/2016 4. If Amendment, Date of Original Filed (Month/Day/Year)								(Check	5. Relationship of Reporting Person(s) to Iss Check all applicable) X Director X Officer (give title below) Chief Executiv 5. Individual or Joint/Group Filling (Check A				X 10% Owner Other (specify below) tive Officer k Applicable Line)		
(Street) SAN FRANCISCO (City)	CA (State)	94 (Zi	i158)		Form filed by On	•	•		
			Т	able I -	Non-Deri	ivative	Securities	Acq	uired, D	ispos	ed of	, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	/Year) if	2A. Deemed Execution Date, f any Month/Day/Year)	Cod	ransaction de (Instr. 8)) (In		ties Acquire 4 and 5)	ed (A) or Dispos	ed Of (D) Price	Ben Foll	mount of Securiti eficially Owned owing Reported saction(s) (Instr.			ership Form: D) or Indirect 7. 4)	7. Nature of Indirect Beneficial Ownership (Instr.
Common Stock					11/28/20	016		1				.091		\$4.025	4)	3,331,639	_		D	4)
						_		+	M				A	• • • •	+		-			
Common Stock					11/28/20			+	S		-,-	399 ⁽¹⁾	D	\$22.74(2)	-	3,312,740	<u> </u>		D	
Common Stock					11/29/20	_		+	M	_		,091	A	\$4.025	-	3,326,831			D	
Common Stock					11/29/20	016		\perp	S		18,8	399 ⁽¹⁾	D	\$22.86 ⁽³⁾		3,307,932			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table I			ecurities Ac							ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securiti	ber of Derivative ies Acquired (A) ed of (D) (Instr.	or	6. Date Exe Expiration (Month/Day	Date	e and		d Amount of Se Security (Instr		lying	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securitie Beneficial Owned	re es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercisabl		iration	Title		Amount or Number of Shares			Followin Reported Transacti (Instr. 4)	d tion(s)		
Stock Option (Right to Buy)	\$4.025	11/28/2015		М			14,091		(5)	02/28	8/2017	Com	nmon Stock	14,09	1	\$0.00	70,45	53	D	
		1				1								1						

				Table II			•	, .	•	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	nstr. 3) Conversion or Exercise (Month/Day/Year) Execution Date, if any Price of (Month/Day/Year)								isable and ate ear)	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	11/29/2016		М			14,091	(5)	02/28/2017	Common Stock	14,091	\$0.00	56,362	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$22.60 to \$23.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$22.50 to \$23.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

11/30/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Report Neff Thomas B	ting Person [*]			2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]											ship of Reporting P applicable) Director	erson(s) t	to Issuer	10% Own	ier	
(Last) C/O FIBROGEN, INC.	(First)	(M	ddle)		3. Date of 12/01/20		t Transaction	n (Monti	n/Day/Year)						X	Officer (give title	below)	cutive O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	, Date of Ori	iginal Fi	led (Month/I	Day/Ye	ear)			6.	Individu X	al or Joint/Group F Form filed by On			•	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	ore than C	One Repo	orting Person	
(City)	(State)	(Zi _l	o)																	
			Т	able I -	Non-Deri	vative	Securitie	es Ac	quired, D	ispo	sed of,	, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact Date	1	2A. Deemed Execution Da		Transaction ode (Instr. 8)		4. Securit (Instr. 3, 4		d (A) or Dispose	ed Of (D)	8	. Amount of Securiti eneficially Owned		Direct (E	rship Form: 0) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		if any (Month/Day/Y	rear) C	ode V		Amount		(A) or (D)	Price		ollowing Reported ransaction(s) (Instr.)	3 and	(I) (Instr.	. 4)	Ownership (Instr. 4)
Common Stock					12/01/2	016			F		4,6	89(1)	D	\$20.5	55	3,303,243			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽²⁾
				Table I			Securities calls, war		,	•	,		cially Owne	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securi	nber of Derivaties Acquired sed of (D) (Ins 5)	d (A) or	6. Date Exe Expiration (Month/Day	Date			d Amount of Sec Security (Instr.		nderlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisable		piration te	Title		Amour Numbe Shares	er of		Owned Followi Reporte Transac (Instr. 4)	ed tion(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/02/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

ı	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person*						nd Ticker or Tra		mbol							nship of Reporting I applicable) Director	Person(s)		X 10% Owr	ner.
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 12/12/20		st Transaction (Month/Da	ay/Year))					X	Officer (give ti	tle below)		Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	, Date of Origir	al Filed	(Month/l	Day/Ye	ear)			(6. Individ	ual or Joint/Group Form filed by 0			•	
(Street) SAN FRANCISCO	CA	94	1158													Form filed by I	More than	One Rep	orting Person	
(City)	(State)	(Z	ip)																	
			Т	able I -	Non-Deri	ivative	Securities	Acqui	ired, D	Dispo	sed of, or	Bene	eficially O	wned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		2A. Deemed Execution Date, if any		nsaction (Instr. 8)		4. Securities <i>F</i> (Instr. 3, 4 and		d (A) or Dispo	sed Of (D		5. Amount of Secu Beneficially Owned Following Reporte	i		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		(Month/Day/Year	Code	v		Amount		(A) or (D)	Price	I·	Transaction(s) (Ins 4)		(i) (inst	r. 4)	Ownership (Instr. 4)
Common Stock					12/12/20	016		М			14,091		A	\$4.0	025	3,317,33	4		D	
Common Stock					12/12/20	016		S			17,999(1	1)	D	\$21.4	45(2)	3,299,33	5		D	
Common Stock					12/12/20	016		S			900(1)		D	\$22.	11(3)	3,298,43	5		D	
Common Stock					12/13/20	016		М			14,091		A	\$4.0	025	3,312,52	6		D	
Common Stock					12/13/20	016		S			16,774(1	1)	D	\$20.	94(4)	3,295,75	2		D	
Common Stock					12/13/20	016		S			2,125(1))	D	\$21.4	46(5)	3,293,62	7		D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁶⁾
				Table			Securities A							ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative		3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	action Code	Securi	nber of Derivativities Acquired (Ased of (D) (Instr	or Ex	Date Exemples Exemples Date Ex	Date	Der		I Amount of S Security (Inst			8. Price of Derivative Security (Inst	Benefi Owned	tive ties cially i	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security							Da	ite	Ex	piration				unt or ber of		Follow Report Transa			

			Code	v	(A)	(D)	Exercisable	Date	Title	Shares		(Instr. 4)		
Stock Option (Right to Buy)	\$4.025	12/12/2016	М			14,091	(7)	02/28/2017	Common Stock	14,091	\$0.00	42,271	D	
Stock Option (Right to Buy)	\$4.025	12/13/2016	М			14,091	(7)	02/28/2017	Common Stock	14,091	\$0.00	28,180	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$21.05 to \$22.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$22.05 to \$22.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$20.45 to \$21.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$21.40 to \$21.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/14/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Report Neff Thomas B	rting Person [*]				2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month/Day/Year)								(Chec	k all ap	Officer (give title be		to Issuer	√ 10% Own	ecify below)	
(Last) C/O FIBROGEN, INC. 409 ILLINOIS ST.	(First)	(M	iddle)		12/27/20 4. If Ame		Date of Origina	al File	ed (Month/l	Day/Yea	ar)						hief Exe		Officer	cony bolowy
(Street) SAN FRANCISCO	CA	94	158													Form filed by On	•	-		
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	vative S	Securities .	Acq	uired, D	Dispos	sed of	, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	. Deemed ecution Date,		ransaction de (Instr. 8)			ties Acquire 4 and 5)	ed (A) or Dispos	sed Of (D)	Ben	mount of Securiti eficially Owned owing Reported	ies		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(monan-bay		onth/Day/Year)	Cod	de V	Aı	mount		(A) or (D)	Price		isaction(s) (Instr.	3 and	(1) (111311)	Ownership (Instr. 4)
Common Stock					12/27/20	016			М		14	,091	A	\$4.025		3,307,718			D	
Common Stock					12/27/20	016			S		18,8	399 ⁽¹⁾	D	\$20.79(2)		3,288,819			D	
Common Stock					12/28/20	016			М		14	,089	A	\$4.025		3,302,908			D	
Common Stock					12/28/20	016			S		18,8	399 ⁽¹⁾	D	\$20.69(3)		3,284,009			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁴⁾
				Table I			curities Ad						icially Owr	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative s Acquired (A) d of (D) (Instr.	or	6. Date Exe Expiration (Month/Day	Date	e and		d Amount of Se Security (Instr		rlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisabl		iration	Title		Amount or Number of Shares			Following Reporte Transaci (Instr. 4)	ed tion(s)		4)
Stock Option (Right to Buy)	\$4.025	12/27/2016		М			14,091		(5)	02/2	28/2017	Com	nmon Stock	14,0	91	\$0.00	14,0)89	D	
		1				1														

				Table II			•	, .	,	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	nstr. 3) Conversion or Exercise Price of Price of Conversion or Exercise Price of Conversion (Month/Day/Year) Execution Date if any (Month/Day/Year)								isable and ate ear)	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	12/28/2016		М			14,089	(5)	02/28/2017	Common Stock	14,089	\$0.00	0	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$20.35 to \$21.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$20.20 to \$20.875. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/29/2016

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep $\underline{NeffThomas\ B}$	orting Person*						id Ticker or Tra		nbol						all ap	p of Reporting Policable) Director	erson(s)	to Issuer		er
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 01/11/20		t Transaction (I	/lonth/Day	y/Year)					X		Officer (give title		ecutive C	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Origin	al Filed (Month/D	ay/Yea	-)			6. Indiv		or Joint/Group F Form filed by On			•	
(Street) SAN FRANCISCO	CA	94	158												F	Form filed by Mo	ore than	One Rep	orting Person	
(City)	(State)	(Z	ip)																	
			Т	able I -	Non-Deri	vative	Securities	Acquir	ed, Di	spose	ed of, or Be	eneficiall	y Own	∍d						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		A. Deemed Execution Date, f any		saction Instr. 8)		Securities Acqu str. 3, 4 and 5)	iired (A) or [isposed	Of (D)	Bene	nount of Securiti eficially Owned owing Reported	es		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		Month/Day/Year	Code	v	Am	ount	(A) or (I) Pr	ce		saction(s) (Instr.	3 and	(i) (ilisti	· *)	Ownership (Instr. 4)
Common Stock					01/11/20	017		M			14,091	A		\$4.025		3,298,100			D	
Common Stock					01/11/20	017		S			10,400(1)	D		\$23.18(2)		3,287,700			D	
Common Stock					01/11/20)17		S			8,499(1)	D		\$23.9 ⁽³⁾		3,279,201			D	
Common Stock					01/12/20	017		М			14,091	A		\$4.025		3,293,292			D	
Common Stock					01/12/20	017		S			9,700(1)	D		\$23.77(4)		3,283,592			D	
Common Stock					01/12/20)17		S			9,199(1)	D		\$24.65(5)		3,274,393			D	
Common Stock																145,070			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁶⁾
				Table			ecurities A						Owned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	action Code	Securit	ber of Derivativ ies Acquired (A ed of (D) (Instr.	or Exp	ate Exer piration [onth/Day/	Date		and Amount			ying	8. Price of Derivative Security (Instr. 5)	9. Num derivati Securit Benefic Owned	ive ies cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security							Dat	e	Expir	ation			Amount or Number of			Followi Reporte Transac	ing ed		7

			Code	V	(A)	(D)	Exercisable	Date	Title	Shares		(Instr. 4)		
Stock Option (Right to Buy)	\$4.025	01/11/2017	М			14,091	(7)	08/20/2017	Common Stock	14,091	\$0.00	271,065	D	
Stock Option (Right to Buy)	\$4.025	01/12/2017	М			14,091	(7)	08/20/2017	Common Stock	14,091	\$0.00	256,974	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$22.75 to \$23.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$23.75 to \$24.125. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$23.45 to \$24.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$24.45 to \$25.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

01/13/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

g Person [*]				FIBRO	GEN I	NC [FGEN]		·)				(Check	all app D	licable) irector			₹ 10% Own	
irst)	(M	ddle)		01/26/20	17								, x	U			cutive (ecity below)
				4. If Amei	ndment, [Date of Origina	al File	ed (Month	/Day/\	rear)					•	٠.		,	
A	94	158												F	orm filed by Mo	re than C	one Rep	orting Person	
State)	(Zi))																	
		Т	able I -	Non-Deri	vative	Securities .	Acq	uired, [Disp	osed of	, or Ben	eficially Ov	vned						
				Date	E	xecution Date,						ed (A) or Dispos	ed Of (D)	Bene	ficially Owned	.	Direct (D) or Indirect	7. Nature of Indirect Beneficial
				(Month/Day/			Cod	de V		Amount		(A) or (D)	Price				(I) (INSTR	. 4)	Ownership (Instr. 4)
				01/26/20	017			М		14	,091	A	\$4.025		3,288,484			D	
				01/26/20	17			S		18,8	8 99 ⁽¹⁾	D	\$23.42(2)		3,269,585			D	
				01/27/20	017			М		14	,091	A	\$4.025		3,283,676			D	
				01/27/20	17			S		18,8	399 ⁽¹⁾	D	\$23.16(3)		3,264,777			D	
															145,070			I	By Family Partnership
															20,000			I	By Spouse
															60,946			I	See footnote ⁽⁴⁾
			Table I				•	,	•	,		•	ed						
2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie Dispose	es Acquired (A) ed of (D) (Instr.	or	Expiration	n Date						Derivative Security (Instr.	derivativ Securitie Benefici	ve es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
Security			Code	v	(A)	(D)					Title		Amount or Number of Shares			Followin Reporte Transact	d tion(s)		,
\$4.025	01/26/2017		M			14,091		(5)	0	8/20/2017	Con	nmon Stock	14,091		\$0.00	242,8	883	D	
	Conversion or Exercise Price of Derivative Security	2. Conversion or Exercise Price of Poerivative Security (Minimize)	2. (Zip) T 2. (Zip) T A 94158 State) (Zip) T A 94158 State) (Zip) T Occurrence of Execution Date of Execution	Table I Conversion or Exercise Price of Derivative Security A 94158 Table I 3. Transaction Date (Month/Day/Year) Fig any (Month/Day/Year) (Month/Day/Year) (Month/Day/Year) (Month/Day/Year)	FIBRO 3. Date of 01/26/20 4. If Amer	FIBROGEN 3. Date of Earliest 01/26/2017 4. If Amendment, 1.	FIBROGEN INC [FGEN 3. Date of Earliest Transaction (No 01/26/2017 4. If Amendment, Date of Origina Table I - Non-Derivative Securities 2. Transaction Date (Month/Day/Year) 01/26/2017 01/26/2017 01/26/2017 01/27/2017 01/27/2017 01/27/2017 21. Derivative Securities Ac (e.g., puts, calls, warrar 22. Ceg., puts, calls, warrar 23. Transaction Date (Month/Day/Year) Price of Derivative Securities Ac (e.g., puts, calls, warrar 24. Code V (A) (D)	FIBROGEN INC [FGEN] 3. Date of Earliest Transaction (Month- 01/26/2017 4. If Amendment, Date of Original File Table I - Non-Derivative Securities Acq 2. Transaction Date (Month/Day/Year) 01/26/2017 01/26/2017 01/26/2017 01/27/2017 01/27/2017 01/27/2017 1. Table II - Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) Table III - Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)	FIBROGEN INC FGEN	FIBROGEN INC	FIBROGEN INC	FIBROGEN INC FGEN	State Care Care	Check X X X X X X X X X	Check all app Check all ap	Check all applicable S. Director Direct	First Check at applicable Check at app	FIBROGEN INC FORM	Part Check all applicable Surface Check all applicable Surface S

				Table II			•	, .	,	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)							Derivative equired (A) or (D) (Instr. 3,	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Amount or Number of Shares			Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	01/27/2017		М			14,091	(5)	08/20/2017	Common Stock	14,091	\$0.00	228,792	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$23.05 to \$23.75. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$22.90 to \$23.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

01/27/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Reportin Neff Thomas B (Last) (F	g Person*	(M	iddle)		FIBRO	GEN IN	icker or Trac]						onship of Reporting R Ill applicable) Director Officer (give title			10% Own Other (sp	ecify below)
	CA State)	94 (Zi	158		4. If Amer	ndment, D <i>a</i>	te of Origina	l Filed	d (Month/Da	y/Year)			6. Indivi	dual or Joint/Group I Form filed by O Form filed by M	ne Reporti	ing Pers	on	
			Т					·	-	<u> </u>	-	eficially Ow						
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day	Year) Exe	Deemed cution Date, by hth/Day/Year)		e (Instr. 8)	4. Securi (Instr. 3,		(A) or Dispos	ed Of (D) Price	5. Amount of Securi Beneficially Owned Following Reported Transaction(s) (Instr 4)	.		ership Form: D) or Indirect . 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
Common Stock					02/08/20	17		N	И	14	1,091	A	\$4.025	3,278,868			D	,
Common Stock					02/08/20	17		S	S	18,	899(1)	D	\$23.03(2)	3,259,969			D	
Common Stock					02/09/20	17		N	И	14	1,091	A	\$4.025	3,274,060			D	
Common Stock					02/09/20	17		S	S	18,	899(1)	D	\$23.89(3)	3,255,161			D	
Common Stock														145,070			I	By Family Partnership
Common Stock														20,000			I	By Spouse
Common Stock														60,946			I	See footnote ⁽⁴⁾
				Table II			urities Ac s, warran					icially Own	ed					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	ction Code	Securities	of Derivative Acquired (A) of (D) (Instr. 3	or E	. Date Exerc expiration Da Month/Day/Y	ate		d Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		ate Exercisable	Expiration Date	Title		Amount or Number of Shares		Followir Reported Transact (Instr. 4)	d tion(s)		,
Stock Option (Right to Buy)	\$4.025	02/08/2017		М			14,091	\perp	(5)	08/20/2017	Com	mon Stock	14,091	\$0.00	214,7	701	D	

				Table II			-			or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)							Derivative equired (A) or (D) (Instr. 3,	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Amount or Number of Shares			Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$4.025	02/09/2017		М			14,091	(5)	08/20/2017	Common Stock	14,091	\$0.00	200,610	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$22.70 to \$23.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$23.55 to \$24.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 5. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

02/10/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person*				FIBRO	GEN IN	Ticker or Trac]						tionship of Reporting P all applicable) Director	erson(s) to Is	suer 10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 02/13/20		ransaction (M	onth/Day/	Year)				X		below) hief Executi	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	l Filed (M	lonth/Day	/Year)			6. Indiv	ridual or Joint/Group F			
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than One	Reporting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	vative S	ecurities /	Acquire	d, Dis	osed of	, or Ben	eficially O	wned				
1. Title of Security (Instr. 3)					2. Transacti Date	Exe	Deemed cution Date,	3. Trans Code (In		4. Securit (Instr. 3,		d (A) or Dispo	sed Of (D)	5. Amount of Securiti	Dire	Ownership Form: ect (D) or Indirect	7. Nature of Indirect
					(Month/Day		nth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 4)		Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					02/13/20	017		М		18	,900	A	\$4.025	3,274,061		D	
Common Stock					02/13/20)17		S		18,9	900(1)	D	\$23.97(2)	3,255,161		D	
Common Stock					02/13/20	017		S		41	8(1)	D	\$24.01 ⁽³⁾	144,652		Ι	By Family Partnership
Common Stock					02/14/20	017		М		18	,900	A	\$4.025	3,274,061		D	
Common Stock					02/14/20	017		S		18,9	900(1)	D	\$23.9(4)	3,255,161		D	
Common Stock					02/14/20)17		S		41	8(1)	D	\$23.89 ⁽⁵⁾	144,234		I	By Family Partnership
Common Stock														20,000		I	By Spouse
Common Stock														60,946		I	See footnote ⁽⁶⁾
				Table I			urities Ac Is, warran						ned				
1. Title of Derivative Security (Instr. 3)	Conversion or Exercise (Month/Day/Year) Execution Date, or Exercise Price of Derivative					Securities	r of Derivative Acquired (A) of (D) (Instr. 3	or Expi	te Exerci ration Da th/Day/Ye			d Amount of S Security (Inst	ecurities Underl . 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr.
D	Security			Code	v	(A)	(D)	Date Exer	cisable	Expiration Date	Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)	(s)	7

Stock Option (Right to Buy)	\$4.025	02/13/2017	M		18,900	(7)	08/20/2017	Common Stock	18,900	\$0.00	181,710	D	
Stock Option (Right to Buy)	\$4.025	02/14/2017	M		18,900	(7)	08/20/2017	Common Stock	18,900	\$0.00	162,810	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$23.70 to \$24.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$23.90 to \$24.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$23.60 to \$24.225. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$23.625 to \$24.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

02/15/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]						Ticker or Trac		ol					onship of Reporting lall applicable)	Person(s) to	Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/06/20		Fransaction (M	onth/Day/Y	'ear)				X	Officer (give titl	•		pecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	Filed (Mo	onth/Day	/Year)			6. Indivi	dual or Joint/Group Form filed by C	• (,	
(Street) SAN FRANCISCO	CA	94	158											Form filed by N	ore than On	e Reporting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Deri	ivative S	Securities A	Acquire	d, Dis	posed of	f, or Ben	eficially Ow	ned				
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day)	Ex	. Deemed ecution Date, any	3. Transa Code (Ins		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	5. Amount of Securi Beneficially Owned Following Reported	D	. Ownership Form: irect (D) or Indirect) (Instr. 4)	7. Nature of Indirect Beneficial
					(MONUMBAY)		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Insti) (IIISU: 4)	Ownership (Instr.
Common Stock					03/06/20	017		F		17,	736(1)	D	\$25.35	3,237,425		D	
Common Stock					03/08/20	017		A		105	,700(2)	A	\$0.00	3,343,125		D	
Common Stock														144,234		I	By Family Partnership
Common Stock														20,000		I	By Spouse
Common Stock														60,946		I	See footnote ⁽³⁾
				Table I			curities Ac Ils, warran					cially Own	ed				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative s Acquired (A) d of (D) (Instr. 3	or Expira	e Exerci ation Da h/Day/Ye			d Amount of Se Security (Instr.	curities Underly 3 and 4)	8. Price of Derivative Security (Instr	9. Number derivative Securities Beneficial Owned	Form: Direct (D) or Indirect	Indirect
	Security			Code	v	(A)	(D)	Date Exerci		Expiration Date	Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)		7
Stock Option (Right to Buy)	\$25.4	03/08/2017		A		172,80	0	(4	4)	03/08/2027	Com	mon Stock	172,800	\$0.00	172,80	0 D	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Represents the grant of restricted stock units. Twenty-five percent of the restricted stock units vest on March 6, 2018, and the remainder vests in equal amounts quarterly thereafter for the following three years.
- 3. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

4. Twenty-five percent of the shares subject to the option vests on March 1, 2018, and the remainder vests in equal amounts quarterly thereafter for the following three years.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/08/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person*						d Ticker or Tra		nbol						onship of Reporting F Il applicable) Director	Person(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of 03/14/20		Transaction (M	/lonth/Da	y/Year)					X	Officer (give title		ecutive O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Origin	al Filed (Month/D	Day/Ye	ear)			6. Individ	ual or Joint/Group I Form filed by O			•	
(Street) SAN FRANCISCO	CA	94	158												Form filed by M	ore than	One Repo	orting Person	
(City)	(State)	(Z	ip)																
			Т	able I -	Non-Deri	vative	Securities	Acquir	red, Di	ispo	sed of, or Ber	neficially C	wned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	E	A. Deemed xecution Date, any		saction Instr. 8)		l. Securities Acquir Instr. 3, 4 and 5)	ed (A) or Disp	osed Of (5. Amount of Securit Beneficially Owned Following Reported			rship Form: D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		any Month/Day/Year	Code	v	Δ	Amount	(A) or (D)	Price		Transaction(s) (Instr 4)		(i) (instr.	. 4)	Ownership (Instr. 4)
Common Stock					03/14/20	017		M			10,858	A	\$4	.025	3,353,983			D	
Common Stock					03/14/20	017		S			18,400(1)	D	\$25	5.04(2)	3,335,583			D	
Common Stock					03/14/20	017		S			500(1)	D	\$25	5.79(3)	3,335,083			D	
Common Stock					03/14/20	017		S			418(1)	D	\$25	5.02(4)	143,816			I	By Family Partnership
Common Stock					03/15/20	017		М			10,858	A	\$4	1.025	3,345,941			D	
Common Stock					03/15/20	017		S			18,900(1)	D	\$25	5.07 ⁽⁵⁾	3,327,041			D	
Common Stock					03/15/20	017		S			418(1)	D	\$25	5.26 ⁽⁶⁾	143,398			D	
Common Stock															20,000			I	By Spouse
Common Stock															60,946			I	See footnote ⁽⁷⁾
				Table							d of, or Bene vertible secur		ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	action Code	Securiti	per of Derivatives Acquired (A) ed of (D) (Instr.	or Exp	Date Exe piration l onth/Day/	Date		nd Amount of Security (Ins			8. Price of Derivative Security (Instr. 5)	9. Num derivati Securit Benefic Owned	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security							Dat	e	Exp	piration			ount or nber of		Follow Reporte	ing ed		"

			Code	v	(A)	(D)	Exercisable	Date	Title	Shares		(Instr. 4)		
Stock Option (Right to Buy)	\$4.025	03/14/2017	М			10,858	(8)	08/20/2017	Common Stock	10,858	\$0.00	151,952	D	
Stock Options (Right to Buy)	\$4.025	03/15/2017	М			10,858	(8)	08/20/2017	Common Stock	10,858	\$0.00	141,094	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$24.70 to \$25.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$25.70 to \$25.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$24.75 to \$25.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$24.55 to \$25.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$25.10 to \$25.375. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/16/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person*					and Ticker or Trac N INC [FGEN		ol				ionship of Reporting Pers all applicable) Director	son(s) to Issuer	10% Ow	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	Middle)		3. Date of Earl 03/20/2017	iest Transaction (M	onth/Day/\	/ear)			X		elow) of Executive C	` '	pecify below)
409 ILLINOIS ST.				4	1. If Amendme	nt, Date of Origina	l Filed (Mo	onth/Day	(Year)		6. Indiv	idual or Joint/Group Filir Form filed by One	•	•	
(Street) SAN FRANCISCO	CA	92	4158									Form filed by More	than One Repo	orting Person	
(City)	(State)	(Z	lip)												
			Т	able I - No	n-Derivati	ve Securities	Acquire	d, Disp	osed of, or Be	neficially C	wned				
1. Title of Security (Instr. 3)	1			Da		2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acqui (Instr. 3, 4 and 5)	red (A) or Disp	osed Of (D)	5. Amount of Securities Beneficially Owned	Direct (I	rship Form: D) or Indirect	7. Nature of Indirect Beneficial
				I (M	lonth/Day/Year	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 : 4)	and (I) (Instr	. 4)	Ownership (Instr.
Common Stock					03/20/2017		М		18,900	A	\$4.025	3,345,941		D	
Common Stock					03/20/2017		S		18,900(1)	D	\$24.88(2)	3,327,041		D	
Common Stock					03/20/2017		S		418(1)	D	\$24.92 ⁽³⁾	142,980		I	By Family Partnership
Common Stock					03/21/2017		М		18,900	A	\$4.025	3,345,941		D	
Common Stock					03/21/2017		S		13,800(1)	D	\$23.51(4)	3,332,141		D	
Common Stock					03/21/2017		S		4,700(1)	D	\$24.54 ⁽⁵⁾	3,327,441		D	
Common Stock					03/21/2017		S		400(1)	D	\$25.06(6)	3,327,041		D	
Common Stock					03/21/2017		S		418(1)	D	\$23.58(7)	142,562		I	By Family Partnership
Common Stock												20,000		I	By Spouse
Common Stock												60,946		I	See footnote ⁽⁸⁾
									sed of, or Bene nvertible secu		ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of		3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transactio	on Code 5. N Sec Dis	umber of Derivative urities Acquired (A) posed of (D) (Instr. 3 ad 5)	6. Dat		sable and 7. Title a	•	Securities Underly	Derivative C Security (Instr. S	erivative ecurities	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Options (Right to Buy)	\$4.025	03/20/2017	M			18,900	(9)	08/20/2017	Common Stock	18,900	\$0.00	122,194	D	
Stock Option (Right to Buy)	\$4.025	03/21/2017	M			18,900	(9)	08/20/2017	Common Stock	18,900	\$0.00	103,294	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$24.55 to \$25.08. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 3. The shares were sold at prices ranging from \$24.80 to \$25.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$23.10 to \$23.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$24.00 to \$24.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 6. The shares were sold at prices ranging from \$25.00 to \$25.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$23.10 to \$24.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/22/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	rting Person [*]						nd Ticker or Tr INC [FGE		Symbol	I						onship of Rep all applicable) Director		erson(s) t	o Issuer	10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o		st Transaction (Month/	'Day/Ye	ear)					X	Officer (g		•	cutive O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	, Date of Origin	nal File	ed (Mon	nth/Day/	/Year)				6. Indivi	dual or Joint/0				•	
(Street) SAN FRANCISCO	CA	94	158														•	•	-	orting Person	
(City)	(State)	(Zi	p)																		
			7	able I -	Non-Der	ivative	Securities	Acq	uired	, Disp	osed o	f, or Ben	eficially C	wnec							
1. Title of Security (Instr. 3)					2. Transact		2A. Deemed Execution Date		ransact de (Inst		4. Securi (Instr. 3,		ed (A) or Disp	sed Of	(D)	5. Amount of Beneficially	Owned		Direct (D	rship Form: 0) or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day/Yea	r) Cod	de	v	Amount		(A) or (D)	Price		Following Re Transaction(s 4)			(I) (Instr.	4)	Beneficial Ownership (Instr. 4)
Common Stock					04/03/2	017		\top	М		18	3,900	A	\$	4.025	3,34	15,941			D	
Common Stock					04/03/2	017			S		18,	900(1)	D	\$2	3.99(2)	3,32	27,041			D	
Common Stock					04/03/2	017			s		4	18 ⁽¹⁾	D	\$2	3.92(3)	14:	2,144			I	By Family Partnership
Common Stock					04/04/2	017			M		18	3,900	A	\$	4.025	3,34	45,941			D	
Common Stock					04/04/2	017			S		18,	900(1)	D	\$2	3.85(4)	3,32	27,041			D	
Common Stock					04/04/2	017			S		4	18(1)	D	\$	23.8 ⁽⁵⁾	14	1,726			I	By Family Partnership
Common Stock																20	,000			I	By Spouse
Common Stock																60	,946			I	See footnote ⁽⁶⁾
				Table I			Securities <i>A</i> calls, warra							ned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securi	nber of Derivati ties Acquired (A sed of (D) (Instr 5)) or	6. Date Expirat (Month/	ion Dat			d Amount of Security (Ins			8. Price Derivati Security 5)	ive y (Instr.	9. Numb derivativ Securitie Benefici Owned	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercis		Expiration Date	Title		Nι	nount or imber of ares			Followin Reporte Transact (Instr. 4)	d tion(s)		ĺ

Stock Options (Right to Buy)	\$4.025	04/03/2017	M		18,900	(7)	08/20/2017	Common Stock	18,900	\$0.00	84,394	D	
Stock Option (Right to Buy)	\$4.025	04/04/2017	M		18,900	(7)	08/20/2017	Common Stock	18,900	\$0.00	65,494	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$23.60 to \$24.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$23.70 to \$24.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$23.60 to \$24.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$23.70 to \$24.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

04/04/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Name and Address of Rep Neff Thomas B	porting Person*					e and Ticker or Trac EN INC [FGEN	0 ,	ol					ionship of Reporting all applicable) Director	Person(s)	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of Ear 04/12/2017	liest Transaction (M	lonth/Day/\	Year)				X		le below) Chief Exe	cutive Of		ecify below)
409 ILLINOIS ST.					4. If Amendm	ent, Date of Origina	l Filed (Mo	onth/Day	/Year)			6. Indivi	idual or Joint/Group Form filed by 0	• •		,	
(Street) SAN FRANCISCO	CA	94	158										Form filed by I	More than (One Repor	rting Person	
(City)	(State)	(Zi	p)														
			Т	able I -	Non-Derivat	ive Securities	Acquire	d, Disp	osed of,	or Ben	eficially O	wned					
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Year	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securitie (Instr. 3, 4		d (A) or Dispo	sed Of (D)	5. Amount of Secur Beneficially Owned Following Reporte	ı		ship Form:) or Indirect 4)	7. Nature of Indirect Beneficial
					(month/buy/real	(Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Ins		(1) (111511.1-	- ,	Ownership (Instr. 4)
Common Stock					04/12/2017		М		18,9	900	A	\$4.025	3,345,94	1		D	
Common Stock					04/12/2017		S		16,60	500 ⁽¹⁾ D \$24		\$24.58 ⁽²⁾	3,329,34	1		D	
Common Stock					04/12/2017		S		2,30	00(1)	D	\$25.28(3)	3,327,04	1		D	
Common Stock					04/12/2017		S		418	3 (1)	D	\$24.57(4)	141,308			I	By Family Partnership
Common Stock					04/13/2017		М		18,9	900	A	\$4.025	3,345,94	1		D	
Common Stock					04/13/2017		S		18,90	00(1)	D	\$24.91 ⁽⁵⁾	3,327,04	1		D	
Common Stock					04/13/2017		S		418	3 (1)	D	\$24.95(6)	140,890			I	By Family Partnership
Common Stock													20,000			I	By Spouse
Common Stock													60,946			I	See footnote ⁽⁷⁾
				Table		e Securities Ac s, calls, warran						ned					
Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative		3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	Sec Dis	Number of Derivative curities Acquired (A) posed of (D) (Instr. : nd 5)	or Expira	te Exercis ation Dat h/Day/Ye	e		d Amount of S Security (Inst	ecurities Underly r. 3 and 4)	8. Price of Derivative Security (Inst	9. Numb derivati r. Securiti Benefic Owned	ive Fies (I	0. Ownership Form: Direct D) or Indirect I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
I	Security							T					 	Followi			" '

			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Reported Transaction(s) (Instr. 4)		
Stock Options (Right to Buy)	\$4.025	04/12/2017	M			18,900	(8)	08/20/2017	Common Stock	18,900	\$0.00	46,594	D	
Stock Option (Right to Buy)	\$4.025	04/13/2017	М			18,900	(8)	08/20/2017	Common Stock	18,900	\$0.00	27,694	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$24.25 to \$24.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$25.00 to \$25.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$24.50 to \$24.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$24.50 to \$25.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$24.65 to \$25.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

04/14/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep $\underline{NeffThomas\ B}$	oorting Person [*]						id Ticker or Tra		ibol						all app	p of Reporting Policable) Director	erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	Middle)		3. Date of 04/24/201		t Transaction (M	lonth/Day	/Year)					X		Officer (give title	below) hief Exe	cutive (Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amer	ndment,	Date of Origina	al Filed (M	Month/D	Day/Ye	ear)			6. Indiv		or Joint/Group F Form filed by On			•	
(Street) SAN FRANCISCO	CA	92	4158												F	Form filed by Mo	ore than (One Rep	orting Person	
(City)	(State)	(Z	ïp)																	
			Т	able I -	Non-Deri	vative	Securities	Acquir	ed, Di	ispo	sed of, or Be	neficially	Owne	d						
1. Title of Security (Instr. 3)					2. Transaction 2A. Deemed Execution Date, (Month/Day/Year) if any						I. Securities Acqu Instr. 3, 4 and 5)	ired (A) or Dis	posed (Of (D)	Bene	mount of Securiti	es	Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day/		f any Month/Day/Year)	Code	v	4	Amount	(A) or (D)	Pric	e		owing Reported saction(s) (Instr.	3 and	(I) (Instr	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					04/24/20	17		М			18,900	A	\top	\$4.025		3,345,941			D	
Common Stock					04/24/20	17		S			18,900(1)	D	1	S26.35 ⁽²⁾		3,327,041			D	
Common Stock					04/24/20	17		S			418(1)	D	\$	\$26.45 ⁽³⁾		140,472			I	By Family Partnership
Common Stock					04/25/20	17		М			8,794	A		\$4.025		3,335,835			D	
Common Stock					04/25/20	17		M			10,106	A		\$2.35		3,345,941			D	
Common Stock					04/25/20	17		S			18,900(1)	D	1	S27.49 ⁽⁴⁾		3,327,041			D	
Common Stock					04/25/20	17		s			418(1)	D	\$	527.67 ⁽⁵⁾		140,054			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁶⁾
				Table I							ed of, or Bene vertible secu		wned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative		3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	action Code	Securit	ber of Derivative ies Acquired (A) ed of (D) (Instr.	or Exp	ate Exe iration I nth/Day/	Date	Derivati	and Amount o			Derivative deriv Security (Instr. Secu		9. Numl derivati Securiti Benefic Owned	ive ies ially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security	1											- 1				Followi			l "

			Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$4.025	04/24/2017	M			18,900	(7)	08/20/2017	Common Stock	18,900	\$0.00	8,794	D	
Stock Option (Right to Buy)	\$4.025	04/25/2017	М			8,794	(7)	08/20/2017	Common Stock	8,794	\$0.00	0	D	
Stock Option (Right to Buy)	\$2.35	04/25/2017	М			10,106	(7)	03/12/2018	Common Stock	10,106	\$0.00	293,813	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$25.95 to \$26.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$26.30 to \$26.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$27.00 to \$27.925. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$27.475 to \$27.925. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini. Attorney-in-fact

04/26/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person*				FIBRO	GEN I	Ticker or Trace NC FGEN Transaction (M]						tionship of Reporting P all applicable) Director	erson(s) to Is	ssuer 10% Owr	ier
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		05/15/20		Transaction (ivi	oniii/Day	real)				X	.0	below) hief Executi		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, [Date of Origina	l Filed (N	lonth/Day	//Year)			6. Indiv	vidual or Joint/Group F	• .		
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than One	Reporting Person	
(City)	(State)	(Zi _l	p)														
			1	Γable I -	Non-Der	ivative	Securities /	Acquire	ed, Dis	posed of	, or Ben	eficially O	wned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Ex	A. Deemed recution Date, any	3. Trans Code (li		4. Securi		d (A) or Dispo	sed Of (D)	5. Amount of Securiti Beneficially Owned Following Reported	Dir	Ownership Form: rect (D) or Indirect (Instr. 4)	7. Nature of Indirect Beneficial
					(Wonth/Day		any lonth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr. 4)		(Instr. 4)	Ownership (Instr. 4)
Common Stock					05/15/20	017		M		18	,900	A	\$2.35	3,345,941		D	
Common Stock					05/15/20	017		S		18,	900 ⁽¹⁾	D	\$27.75 ⁽²⁾	3,327,041		D	
Common Stock					05/15/20	017		S		41	18(1)	D	\$27.81 ⁽³⁾	139,636	139,636		By Family Partnership
Common Stock					05/16/20	017		М		18	,900	A	\$2.35	3,345,941		D	
Common Stock					05/16/20	017		S		18,	900(1)	D	\$27.64(4)	3,327,041		D	
Common Stock					05/16/20	017		S		41	18(1)	D	\$27.67 ⁽⁵⁾	139,218		I	By Family Partnership
Common Stock														20,000		Ι	By Spouse
Common Stock														60,946		I	See footnote ⁽⁶⁾
				Table I			curities Ac						ned				
Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative es Acquired (A) d of (D) (Instr. 3	or Expi	ate Exerci ration Da ath/Day/Ye			d Amount of S Security (Inst		sities Underlying and 4) 8. Price of Derivative Security (Instr. 5) 9. Number of derivative Securities Beneficially Owned 10. Ownership Form: Direct (D) or Indirect Beneficially Owned (I) (Instr. 4) 4) 4)			
	Security			Code	v	(A)	(D)	Date Exer	cisable	Expiration Date	Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)	n(s)	•,

Stock Option (Right to Buy)	\$2.35	05/15/2017	M		18,900	(7)	03/12/2018	Common Stock	18,900	\$0.00	274,913	D	
Stock Option (Right to Buy)	\$2.35	05/16/2017	M		18,900	(7)	03/12/2018	Common Stock	18,900	\$0.00	256,013	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$27.45 to \$27.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$27.70 to \$27.875. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$27.35 to \$27.875. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$27.40 to \$27.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ John Alden, Attorney-in-fact

05/17/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person*				ne and Ticker or Tra EN INC [FGEN		ol				ionship of Reporting Persor all applicable) Director	n(s) to Issuer	vner
(Last) C/O FIBROGEN, INC.	(First)	(Mi	iddle)	3. Date of Ea 05/30/2017	rliest Transaction (N	lonth/Day/\	Year)			X	Officer (give title belo		specify below)
409 ILLINOIS ST.				4. If Amenda	nent, Date of Origina	al Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filing Form filed by One Re	` '' '	
(Street) SAN FRANCISCO	CA	941	158								Form filed by More th	nan One Reporting Person	
(City)	(State)	(Zip	o)										
			Ta	able I - Non-Deriva	tive Securities	Acquire	d, Dis	posed of, or Be	eneficially O	wned			
1. Title of Security (Instr. 3)				2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acqu (Instr. 3, 4 and 5)	uired (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
				(Month/Day/Yea	r) if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock				05/30/2017		М		18,900	A	\$2.35	3,345,941	D	
Common Stock				05/30/2017		S		11,400(1)	D	\$26.16 ⁽²⁾	3,334,541	D	
Common Stock				05/30/2017		S		7,500(1)	D	\$26.88(3)	3,327,041	D	
Common Stock				05/30/2017		S		418(1)	D	\$26.3(4)	138,800	I	By Family Partnership
Common Stock				05/31/2017		М		18,900	A	\$2.35	3,345,941	D	
Common Stock				05/31/2017		S		18,900(1)	D	\$25.97(5)	3,327,041	D	
Common Stock				05/31/2017		S		418(1)	D	\$26.03(6)	138,382	I	By Family Partnership
Common Stock				06/01/2017		F		4,689 ⁽⁷⁾	D	\$27.6	3,322,352	D	
Common Stock											20,000	I	By Spouse
Common Stock											60,946	I	See footnote ⁽⁸⁾
				Table II - Derivativ (e.g., put	e Securities Ac s, calls, warran					ned			
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	4. Transaction Code (Instr. 8) Se	Number of Derivative curities Acquired (A) sposed of (D) (Instr. and 5)	6. Dat		sable and 7. Title te Derivat	-	Securities Underly tr. 3 and 4)	Derivative der Security (Instr. Sec	Number of ivative Form: Direct (D) or Indirect (elicities (I) (I) (Instr. 4)	Indirect		

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.35	05/30/2017	M			18,900	(9)	03/12/2018	Common Stock	18,900	\$0.00	237,113	D	
Stock Option (Right to Buy)	\$2.35	05/31/2017	M			18,900	(9)	03/12/2018	Common Stock	18,900	\$0.00	218,213	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$25.70 to \$26.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$26.70 to \$27.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$25.85 to \$26.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$25.35 to \$26.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$25.75 to \$26.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/01/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]						and Ticker o	,	g Symbol							hip of Reporting Populicable)	erson(s) to	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/06/20		st Transacti	tion (Mont	h/Day/Yea	r)					X	Officer (give title	below)	cutive Of		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	t, Date of O	Original F	iled (Month	n/Day/`	Year)			6.	Individua <mark>X</mark>	or Joint/Group F				
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	ore than O	ne Repo	rting Person	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	vativ	e Securit	ties Ac	quired,	Disp	osed of	, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact Date		2A. Deemed Execution D		Transactio		4. Securit (Instr. 3,		d (A) or Dispose	ed Of (D)	Be	5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and		or Indirect	7. Nature of Indirect	
					(Month/Day		if any (Month/Day/	y/Year) c	ode \	,	Amount		(A) or (D)	Price				(I) (Instr. 4	4)	Beneficial Ownership (Instr. 4)
Common Stock					06/06/2	017			F		3,2	61(1)	D	\$29.0)5	3,319,091			D	
Common Stock																138,382			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽²⁾
				Table I			Securitie: calls, wa		,	•	,		cially Owne ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securi	mber of Deri ities Acquire sed of (D) (I 5)	red (A) or	6. Date E Expiratio (Month/D	n Date	.		d Amount of Sec Security (Instr.		nderlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Beneficia	re F	0. Ownership Form: Direct D) or Indirect I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D))	Date Exercisal		xpiration ate	Title		Amoun Numbe Shares	r of		Owned Followin Reported Transact (Instr. 4)	d tion(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/08/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	rting Person [*]						nd Ticker or Tr		Symbol							onship of Report all applicable) Director	ng Persoi	n(s) to Iss	uer 10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 06/15/20		st Transaction (Month/I	Day/Ye	ar)					X	Officer (give		ow) Executiv	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	, Date of Origin	nal File	d (Mont	th/Day/	Year)				6. Individ	dual or Joint/Gro				
(Street) SAN FRANCISCO	CA	94	158														-		Reporting Person	
(City)	(State)	(Zi	p)																	
			7	able I -	Non-Der	ivative	e Securities	Acqı	uired,	, Disp	osed of	, or Ben	eficially C	wnec	l					
1. Title of Security (Instr. 3)					2. Transac		2A. Deemed Execution Date		ransacti le (Instr		4. Securi		d (A) or Disp	osed Of	(D)	5. Amount of Se Beneficially Ow	ned	Direc	wnership Form: ct (D) or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day/Yea	r) Cod	de	v	Amount		(A) or (D)	Price		Following Report Transaction(s) (4)			nstr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					06/15/2	017		1	М		11	,689	A	1	\$2.35	3,330,	780		D	
Common Stock					06/15/2	017			S		18,	900(1)	D	\$2	29.25 ⁽²⁾	3,311,	880		D	
Common Stock					06/15/2	017			S		41	18(1)	D	\$2	9.28(3)	137,9	64		I	By Family Partnership
Common Stock					06/16/2	017		1	M		18	,900	A	,	\$2.35	3,330,	780		D	
Common Stock					06/16/2	017			S		18,	900(1)	D	\$2	.9.54 ⁽⁴⁾	3,311,	880		D	
Common Stock					06/16/2	017			S		41	18(1)	D	\$2	29.58 ⁽⁵⁾	137,5	46		I	By Family Partnership
Common Stock																20,00	00		I	By Spouse
Common Stock																60,94	16		I	See footnote ⁽⁶⁾
				Table I			Securities A calls, warra							ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securi	nber of Derivati ties Acquired (A sed of (D) (Instr 5)	or E	6. Date I Expirati (Month/I	on Date			d Amount of Security (Ins			8. Price of Derivative Security (I	der nstr. Sed Ber	Number of rivative curities neficially vned	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Νι	nount or imber of iares		Fol Rep Tra	llowing ported ansaction(s str. 4)	s)	ĺ

Stock Option (Right to Buy)	\$2.35	06/15/2017	M		11,689	(7)	03/12/2018	Common Stock	11,689	\$0.00	206,524	D	
Stock Option (Right to Buy)	\$2.35	06/16/2017	M		18,900	(7)	03/12/2018	Common Stock	18,900	\$0.00	187,624	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$28.65 to \$29.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$29.15 to \$29.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$29.15 to \$29.75. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$29.45 to \$29.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/19/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person*					me and Ticker of EN INC [F			ol					ionship of Reporting Pe all applicable) Director	erson(s) to I	ssuer 10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	1iddle)		3. Date of E 06/21/2017	arliest Transact	ion (M	onth/Day/\	∕ear)				X			Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amend	ment, Date of C	Origina	Filed (Mo	onth/Day	/Year)			6. Indiv	dual or Joint/Group Fi	• .		
(Street) SAN FRANCISCO	CA	94	4158											Form filed by Mo	re than One	e Reporting Person	
(City)	(State)	(Z	ip)														
			Т	able I -	Non-Deriv	ative Securi	ties A	Acquire	d, Dis	posed of, o	r Bene	eficially O	wned				
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Ye	Execution I		3. Transa Code (Ins		4. Securities (Instr. 3, 4 an		d (A) or Dispo	osed Of (D)	5. Amount of Securitien Beneficially Owned Following Reported	Di	Ownership Form: rect (D) or Indirect (Instr. 4)	7. Nature of Indirect Beneficial
					(Month/Day/Y	ear) if any (Month/Day	/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Instr. 3		(Instr. 4)	Ownership (Instr.
Common Stock					06/21/201	7		M		18,900)	A	\$2.35	3,330,780		D	
Common Stock					06/21/201	7		S		18,900	(1)	D	\$ 31.15 ⁽²⁾	3,311,880		D	
Common Stock					06/21/201	7		S		418(1))	D	\$31.22(3)	137,128		I	By Family Partnership
Common Stock					06/22/201	7		M		18,900)	A	\$2.35	3,330,780		D	
Common Stock					06/22/201	7		S		16,700	(1)	D	\$31.82(4)	3,314,080		D	
Common Stock					06/22/201	7		S		2,200(1	1)	D	\$32.31(5)	3,311,880		D	
Common Stock					06/22/201	7		S		418(1))	D	\$32.02(6)	136,710		I	By Family Partnership
Common Stock														20,000		I	By Spouse
Common Stock														60,946		I	See footnote ⁽⁷⁾
				Table I		ve Securitie ıts, calls, wa							ned				
1. Title of Derivative Security (Instr. 3)					8	i. Number of Der Securities Acquir Disposed of (D) (and 5)	ed (A)	or Expira	e Exerci ation Da h/Day/Ye	te De		d Amount of S Security (Inst	Securities Underly tr. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficiall Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr.
l	Security														Following		4)

			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$2.35	06/21/2017	М			18,900	(8)	03/12/2018	Common Stock	18,900	\$0.00	168,724	D	
Stock Option (Right to Buy)	\$2.35	06/22/2017	М			18,900	(8)	03/12/2018	Common Stock	18,900	\$0.00	149,824	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$30.70 to \$31.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$30.90 to \$31.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$31.15 to \$32.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$32.15 to \$32.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$31.85 to \$32.425. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/23/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person*			and Ticker or Trac NINC [FGEN		ol				ionship of Reporting Person(s all applicable) Director	s) to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 07/06/2017	est Transaction (M	onth/Day/Y	′ear)			X		Other (s	pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filing (0 Form filed by One Rep		
(Street) SAN FRANCISCO	CA	94158									n One Reporting Person	
(City)	(State)	(Zip)										
		Т	able I - Non-Derivativ	e Securities /	Acquire	d, Disp	oosed of, or Bei	neficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	red (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)		
Common Stock			07/06/2017		M		18,900	A	\$2.35	3,330,780	D	
Common Stock			07/06/2017		S		9,300(1)	D	\$33.27(2)	3,321,480	D	
Common Stock			07/06/2017		S		9,600(1)	D	\$33.79(3)	3,311,880	D	
Common Stock			07/06/2017		S		218(1)	D	\$33.23(4)	136,492	I	By Family Partnership
Common Stock			07/06/2017		S		200(1)	D	\$33.78(5)	136,292	I	By Family Partnership
Common Stock			07/07/2017		M		18,900	A	\$2.35	3,330,780	D	
Common Stock			07/07/2017		S		18,900(1)	D	\$33.22(6)	3,311,880	D	
Common Stock			07/07/2017		S		418(1)	D	\$33.24 ⁽⁷⁾	135,874	I	By Family Partnership
Common Stock										20,000	I	By Spouse
Common Stock										60,946	I	See footnote ⁽⁸⁾
			Table II - Derivative		. ,	•	sed of, or Bene	•	ned			
Title of Derivative Security (Instr. 3)	Conversion	3. Transaction 3A. Deemed Execution Date, if any	4. Transaction Code (Instr. 8) 5. No	imber of Derivative rities Acquired (A) osed of (D) (Instr. 3	6. Date	e Exercis	sable and 7. Title a		Securities Underly tr. 3 and 4)	ying 8. Price of 9. Nu Derivative derivative Security (Instr. Security		Indirect

1	Price of		(Month/Day/Year)			4 and 5)						5)		(I) (Instr. 4)	Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.35	07/06/2017		M			18,900	(9)	03/12/2018	Common Stock	18,900	\$0.00	130,924	D	
Stock Option (Right to Buy)	\$2.35	07/07/2017		M			18,900	(9)	03/12/2018	Common Stock	18,900	\$0.00	112,024	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$32.70 to \$33.675. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$33.70 to \$34.175. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$32.75 to \$33.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$33.75 to \$33.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$32.85 to \$33.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 7. The shares were sold at prices ranging from \$33.00 to \$33.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners. LP. The reporting person is the sole general partner of BioGrowth Partners. LP and has sole voting and dispositive power over the shares held by BioGrowth Partners. LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/07/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

l	OMB APPROVAL	
	OMB Number:	3235-0287
	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person [*]				FIBRO	GEN IN	Ticker or Trac]						tionship of Reporting P all applicable) Director	erson(s) to Is	ssuer 10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		07/24/20		ransaction (M	ontn/Day/	Year)				X		below) hief Execut		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	Filed (M	onth/Day	//Year)			6. Indiv	idual or Joint/Group F Form filed by On		• • • • • • • • • • • • • • • • • • • •	
(Street) SAN FRANCISCO	CA	94	158											Form filed by Mo	ore than One	Reporting Person	
(City)	(State)	(Zi	p)														
			1	able I -	Non-Deri	vative S	ecurities A	Acquire	d, Dis	posed of	, or Ben	eficially O	wned				
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day	Exe	Deemed ecution Date,	3. Transa Code (In		4. Securi		ed (A) or Dispo	sed Of (D)	5. Amount of Securiti Beneficially Owned	Dii	Ownership Form: rect (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		ny onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Following Reported Transaction(s) (Instr. 4)		(Instr. 4)	Ownership (Instr. 4)
Common Stock					07/24/20	017		M		18	,900	A	\$2.35	3,330,780		D	
Common Stock					07/24/20	017		S		18,	900(1)	D	\$35.06 ⁽²⁾	3,311,880		D	
Common Stock					07/24/20	017		S		41	[8 ⁽¹⁾	D	\$35.09 ⁽³⁾	135,456		I	By Family Partnership
Common Stock					07/25/20	017		M		18	,900	A	\$2.35	3,330,780		D	
Common Stock					07/25/20	017		S		18,	900(1)	D	\$35.12(4)	3,311,880		D	
Common Stock					07/25/20	017		S		41	18(1)	D	\$35.11 ⁽⁵⁾	135,038		I	By Family Partnership
Common Stock														20,000		I	By Spouse
Common Stock														60,946		I	See footnote ⁽⁶⁾
				Table I			curities Ac	. ,		,		icially Owi	ned				
1. Title of Derivative Security (Instr. 3)							r of Derivative Acquired (A) of (D) (Instr. 3	or Expir	te Exerci ation Da th/Day/Ye			d Amount of S Security (Inst	ecurities Underl r. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficially Owned	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Derivative Security					(A)	(D)	Date Exerc	cisable	Expiration Date	Title		Amount or Number of Shares		Following Reported Transaction (Instr. 4)	n(s)	-*·)

Stock Option (Right to Buy)	\$2.35	07/24/2017	M		18,900	(7)	03/12/2018	Common Stock	18,900	\$0.00	93,124	D	
Stock Option (Right to Buy)	\$2.35	07/25/2017	M		18,900	(7)	03/12/2018	Common Stock	18,900	\$0.00	74,224	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$34.75 to \$35.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$34.75 to \$35.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$34.55 to \$35.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$34.85 to \$35.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/26/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Name and Address of Reporting Person* Neff Thomas B					2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]										nship of Reporting I I applicable) Director	. ,		10% Owr	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		Date of Earliest Transaction (Month/Day/Year) 08/28/2017									X	Officer (give title	e below) Chief Exe	ecutive (ecify below)	
409 ILLINOIS ST.	4. If Amendment, Date of Original Filed (Month/Day/Year)										Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person									
(Street) SAN FRANCISCO	CA	94	1158												Form filed by M	lore than	One Rep	orting Person		
(City)	(State)	(Z	ip)																	
			Т	able I -	Non-Deri	ative Se	curities A	Acquire	d, Disp	osed of	f, or Ben	eficially O	wned							
1. Title of Security (Instr. 3)					2. Transacti Date	Exec	eemed ution Date,	3. Transa Code (In		4. Securi		d (A) or Dispo	sed Of (I	í [:	5. Amount of Securi Beneficially Owned		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial Ownership (Instr. 4)	
					(Month/Day/		y th/Day/Year)	Code	v	Amount		(A) or (D)	Price	- 1	Following Reported Transaction(s) (Instr. 3 and 4)					
Common Stock					08/28/20	17		М		18	3,900	A	\$2	2.35	3,330,780			D		
Common Stock					08/28/20	17		S		18,	900(1)	D	\$43	.04(2)	3,311,880			D		
Common Stock					08/28/20	17		S		41	18(1)	D	\$43	3.1 ⁽³⁾	134,620			I	By Family Partnership	
Common Stock					08/29/20	17		М		17	,524	A	\$2	2.35	3,329,404			D		
Common Stock					08/29/20	17		S		3,1	.00(1)	D	\$43	.43(4)	3,326,304			D		
Common Stock					08/29/20	17		S		15,	800(1)	D	\$44	1.6(5)	3,310,504			D		
Common Stock					08/29/20	17		S		41	18(1)	D	\$44	.64(6)	134,202			I	By Family Partnership	
Common Stock															20,000			I	By Spouse	
Common Stock													60,94		6		I	See footnote ⁽⁷⁾		
				Table I			urities Ac s, warran					icially Owr	ned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	Execution Date,		ction Code	Securities	Number of Derivative curities Acquired (A) of sposed of (D) (Instr. 3		or Expiration Dat		7. Title and Amount of Securit Derivative Security (Instr. 3 an				8. Price of Derivative Security (Instr	9. Num derivat Securit Benefic Owned Follow	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	

			Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$2.35	08/28/2017	М			18,900	(8)	03/12/2018	Common Stock	18,900	\$0.00	55,324	D	
Stock Option (Right to Buy)	\$2.35	08/29/2017	М			17,524	(8)	03/12/2018	Common Stock	17,524	\$0.00	37,800	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$42.80 to \$43.425. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$42.85 to \$43.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$43.05 to \$43.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$44.00 to \$44.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$44.45 to \$44.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/30/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	tina Danaa*				2 leguer N	Jame an	nd Ticker or Ti	adino	Symbol					5	Palations	hip of Reporting P	ereon(e) f	to lecuar		
Neff Thomas B	ung Person						INC [FGE		Oymbor						heck all a	applicable) Director	013011(3)	10 133001	10% Own	
							t Transaction	(Montl	h/Day/Yea	ır)					X X	Officer (give title	helow)			ecify below)
(Last)	(First)	(M	iddle)		09/01/20	17									Λ		,	cutive Of		ecity below)
C/O FIBROGEN, INC.							5				., .									
409 ILLINOIS ST.					4. If Amei	ndment,	, Date of Origi	nal Fi	led (Monti	n/Day/	Year)			6.	Individua X	I or Joint/Group F Form filed by Or			•	
(Street)																Form filed by Mo	-	-		
SAN FRANCISCO	CA	94	158																	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	vative	Securities	Ac	quired,	Disp	osed of	, or Ben	eficially Ov	/ned						
1. Title of Security (Instr. 3)					2. Transact Date		2A. Deemed Execution Date		Transaction		4. Securi (Instr. 3,		d (A) or Dispos	ed Of (D)	Be	Amount of Securit			or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day/Yea	ar) c	ode	/	Amount		(A) or (D)	Price		ollowing Reported ansaction(s) (Instr.		(I) (Instr. 4	•)	Beneficial Ownership (Instr. 4)
Common Stock					09/01/20	017			F		4,6	588(1)	D	\$49		3,305,816			D	
Common Stock					09/06/20	017			F		3,2	261(1)	D	\$48.	1	3,302,555			D	
Common Stock																134,202			I	By Family Partnership
Common Stock																20,000			Ι	By Spouse
Common Stock																60,946			I	See footnote ⁽²⁾
				Table I			Securities A						icially Own ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securit	nber of Derivat ties Acquired (sed of (D) (Inst 5)	A) or	6. Date E Expiratio (Month/D	n Date	•		d Amount of Se Security (Instr.		nderlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivati Securiti Benefic	ve Feies (Eially (I)	D. Ownership orm: Direct D) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Amoun Numbe Shares	r of		Owned Followi Reporte Transac (Instr. 4)	ng ed ction(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re	eporting Person*			and Ticker or Trac		ol			(Check	tionship of Reporting Person(s)) to Issuer	
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 09/13/2017	est Transaction (M	onth/Day/\	'ear)) X	Officer (give title below)		ner pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	onth/Day	/Year)		6. Indi	vidual or Joint/Group Filing (C		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)	_									
		Table I	- Non-Derivati	ve Securities /	Acquire	d, Disp	osed of, or Ber	neficially O	vned			
1. Title of Security (Instr. 3)		2. Transaction Date		3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			09/13/2017		S		4,900(1)	D	\$50.33(2)	3,297,655	D	
Common Stock			09/13/2017		S		11,500 ⁽¹⁾	D	\$51.52 ⁽³⁾	3,286,155	D	
Common Stock			09/13/2017		S		2,500(1)	D	\$52.13 ⁽⁴⁾	3,283,655	D	
Common Stock			09/13/2017		S		318(1)	D	\$51.75	133,884	I	By Family Partnership
Common Stock			09/13/2017		s		100(1)	D	\$51.275	133,784	I	By Family Partnership
Common Stock			09/14/2017		S		1,500(1)	D	\$50.89 ⁽⁵⁾	3,282,155	D	
Common Stock			09/14/2017		S		12,000(1)	D	\$51.99 ⁽⁶⁾	3,270,155	D	
Common Stock			09/14/2017		S		5,400(1)	D	\$52.47 ⁽⁷⁾	3,264,755	D	
Common Stock			09/14/2017		S		318(1)	D	\$52.075	133,466	I	By Family Partnership
Common Stock			09/14/2017		S		100(1)	D	\$51.55	133,366	I	By Family Partnership
Common Stock										20,000	I	By Spouse
Common Stock										60,946	I	See footnote ⁽⁸⁾

				Table II			•		,	or Beneficially Owne e securities)	d				
1. Title of Derivative Security (Instr. 3)	Price of	Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)		5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ate	7. Title and Amount of Seco Derivative Security (Instr. 3		Derivative Security (Instr.	Securities Beneficially	(D) or Indirect	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan
- 2. The shares were sold at prices ranging from \$49.60 to \$50.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$50.95 to \$51.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$51.95 to \$52.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$50.30 to \$51.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$51.35 to \$52.325. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$52.35 to \$52.625. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/15/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Rep Neff Thomas B	orting Person*						Ticker or Trac	,	nbol					eck all a	nip of Reporting Popplicable) Director	erson(s) to Iss	suer 10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/19/20		ransaction (M	onth/Da	y/Year)						Officer (give title	below) hief Executiv	Other (sp	pecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	l Filed (Month/Da	//Year)			6. Ir		or Joint/Group F Form filed by On	• •	,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than One	Reporting Person	
(City)	(State)	(Zi	p)															
			Т	able I -	Non-Deri	vative S	Securities A	A cquii	red, Dis	posed of	f, or Ben	eficially O	wned					
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day	Ex	Deemed ecution Date,		saction Instr. 8)	4. Securi (Instr. 3,		ed (A) or Dispo	sed Of (D)	Ber	Amount of Securiti neficially Owned llowing Reported	Dire	wnership Form: ct (D) or Indirect nstr. 4)	7. Nature of Indirect Beneficial
					,	(M	onth/Day/Year)	Code	v	Amount		(A) or (D)	Price	Tra 4)	insaction(s) (Instr.	3 and	•	Ownership (Instr. 4)
Common Stock					09/19/20)17		S		18,	001(1)	D	\$53.22	2)	3,246,754		D	
Common Stock					09/19/20)17		S		89	99(1)	D	\$53.71	3)	3,245,855		D	
Common Stock					09/19/20)17		S		4	18(1)	D	\$52.85(4)	132,948		I	By Family Partnership
Common Stock					09/20/20)17		S		18,	900(1)	D	\$53.69(5)	3,226,955		D	
Common Stock					09/20/20)17		S		4:	18(1)	D	\$53.48(6)	132,520		I	By Family Partnership
Common Stock															20,000		I	By Spouse
Common Stock															60,946		I	See footnote ⁽⁷⁾
				Table I			curities Ac					icially Owr	ned					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	er of Derivative s Acquired (A) I of (D) (Instr. 3	or Exp	Date Exerc piration Da onth/Day/Yo	te		d Amount of S Security (Inst		derlying	8. Price of Derivative Security (Instr. 5)	9. Number o derivative Securities Beneficially Owned	f 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security			Code	v	(A)	(D)	Dat Exe		Expiration Date	Title		Amount Number Shares			Following Reported Transaction((Instr. 4)	s)	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$52.70 to \$53.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$53.70 to \$53.75. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$52.75 to \$53.175. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$53.10 to \$53.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$53.15 to \$53.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

09/21/2017

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person*				FIBROG	ne and Ticker or Trac EN INC [FGEN]					tionship of Reporting Person all applicable) Director	(s) to Issuer	/ner
(Last) C/O FIBROGEN, INC.	(First)	(N	liddle)		3. Date of Ea 10/02/2017	rliest Transaction (M	onth/Day/Y	'ear)			X		w) Other (s Executive Officer	pecify below)
409 ILLINOIS ST.					4. If Amenda	nent, Date of Origina	l Filed (Mo	nth/Day	Year)		6. Indiv	ridual or Joint/Group Filing (Form filed by One Re		
(Street) SAN FRANCISCO	CA	94	1158									Form filed by More tha	an One Reporting Person	
(City)	(State)	(Z	ip)											
			Т	able I - I	Non-Deriva	tive Securities	Acquire	d, Disp	osed of, or B	Seneficially C	Owned			
1. Title of Security (Instr. 3)					2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acc (Instr. 3, 4 and 5	quired (A) or Disp)	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
					(Month/Day/Yea	r) if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					10/02/2017		S		9,500(1)	D	\$54.12 ⁽²⁾	3,217,455	D	
Common Stock					10/02/2017		S		9,400(1)	D	\$54.78(3)	3,208,055	D	
Common Stock					10/02/2017		S		318(1)	D	\$55.3	132,212	I	By Family Partnership
Common Stock					10/02/2017		S		100(1)	D	\$53.8	132,112	I	By Family Partnership
Common Stock					10/03/2017		S		18,900(1)	D	\$55.71(4)	3,189,155	D	
Common Stock					10/03/2017		S		318(1)	D	\$55.95	131,794	I	By Family Partnership
Common Stock					10/03/2017		S		100(1)	D	\$55.65	131,694	I	By Family Partnership
Common Stock												20,000	I	By Spouse
Common Stock												60,946	I	See footnote ⁽⁵⁾
				Table I		e Securities Ac					ned			
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of		3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code 5.	Number of Derivative curities Acquired (A) sposed of (D) (Instr. 3 and 5)	6. Dat		sable and 7. Title		Securities Underl tr. 3 and 4)	Derivative deri Security (Instr. Sec	umber of vative urities eficially 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect

l l Dor	rivative	1	1							1		ı	Owned	I	l 4)	1
	curity												Following		"	-
											Amount or		Reported		1	-
		ı						Date	Expiration		Number of		Transaction(s)		1	
				Code	V	(A)	(D)	Exercisable	Date	Title	Shares		(Instr. 4)		1	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$53.50 to \$54.475. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$54.50 to \$55.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$55.15 to \$55.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

10/04/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re $\underline{Neff\ Thomas\ B}$	eporting Person*			Name and Ticker or Tr OGEN INC [FGE		ool				tionship of Reporting Person(all applicable) Director	s) to Issuer 10% Ov	vner			
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of 10/16/20	f Earliest Transaction (117	Month/Day/	Year)				X Officer (give title below) Other (specify below) Chief Executive Officer					
409 ILLINOIS ST.			4. If Ame	ndment, Date of Origi	nal Filed (M	onth/Day	r/Year)		6. Indiv	ridual or Joint/Group Filing (C					
(Street) SAN FRANCISCO	CA	94158								Form filed by More tha	n One Reporting Person				
(City)	(State)	(Zip)													
			Table I - Non-Der	ivative Securities	Acquire	d, Dis	posed of, or Be	neficially C	wned						
1. Title of Security (Instr. 3)		2. Transac Date	Execution Date	3. Transa Code (In		4. Securities Acqui (Instr. 3, 4 and 5)	red (A) or Disp	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect			
			(Month/Day	/Year) if any (Month/Day/Yea	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Inst 4)			
Common Stock			10/16/2	017	S		12,294(1)	D	\$54.54(2)	3,176,861	D				
Common Stock			10/16/2	017	S		6,606(1)	D	\$55.37(3)	3,170,255	D				
Common Stock			10/16/2	017	S		417(1)	D	\$54.35 ⁽⁴⁾	131,277	I	By Family Partnership			
Common Stock			10/16/2	017	S		1(1)	D	\$55.45	131,276	I	By Family Partnership			
Common Stock			10/17/2	017	S		4,200(1)	D	\$54.69 ⁽⁵⁾	3,166,055	D				
Common Stock			10/17/2	017	S		14,700(1)	D	\$55.38(6)	3,151,355	D				
Common Stock			10/17/2	017	S		100(1)	D	\$55.1	131,176	I	By Family Partnership			
Common Stock			10/17/2	017	S		318(1)	D	\$55.25	130,858	I	By Family Partnership			
Common Stock										20,000	I	By Spouse			
Common Stock										60,946	I	See footnote(
				ative Securities A puts, calls, warra					ned						
1. Title of Derivative Securit	y 2.	3. Transaction 3A. Deemed		5. Number of Derivati					Securities Under	lying 8. Price of 9. Nu	mber of 10. Ownership	11. Nature of			

, ,	Price of	(Month/Day/Year)	(Instr. 8)		Securities Ac Disposed of (4 and 5)		Expiration Da (Month/Day/Y		Derivative Security (Instr. 3		Security (Instr.	Securities Beneficially	(D) or Indirect	Indirect Beneficial Ownership (Instr.
	Derivative Security									Amount or		Owned Following Reported		4)
			Code	v	(A)	(D)	Date Exercisable	Expiration Date		Number of Shares		Transaction(s) (Instr. 4)		

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$54.10 to \$55.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$55.15 to \$56.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$54.30 to \$54.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$54.00 to \$55.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$55.05 to \$55.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

10/18/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person*			<u>F</u>	FIBROGEN	and Ticker or Trad]					tionship of Reporting Person(all applicable) Director	10% Owner		
(Last) C/O FIBROGEN, INC.	(First)	(Mid	ddle)		3. Date of Earlie 10/30/2017	est Transaction (Mo	onth/Day/Y	'ear)			X		Other (s executive Officer	pecify below)	
409 ILLINOIS ST.				4	I. If Amendmer	t, Date of Original	Filed (Mo	nth/Day	Year)		6. Indiv	idual or Joint/Group Filing (Form filed by One Rep			
(Street) SAN FRANCISCO	CA	941	158									Form filed by More tha	n One Reporting Person		
(City)	(State)	(Zip))												
			Т	able I - No	n-Derivativ	e Securities A	cquire	d, Disp	osed of, or Ber	eficially O	wned				
1. Title of Security (Instr. 3)				Da		2A. Deemed Execution Date,	3. Transac Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect Beneficial	
				(Me	ontn/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Ownership (Instr.	
Common Stock					10/30/2017		S		6,782(1)	D	\$55.79(2)	3,144,573	D		
Common Stock					10/30/2017		S		9,918(1)	D	\$56.65(3)	3,134,655	D		
Common Stock					10/30/2017		S		2,200(1)	D	\$57.36(4)	3,132,455	D		
Common Stock					10/30/2017		S		408(1)	D	\$55.82 ⁽⁵⁾	130,450	I	By Family Partnership	
Common Stock					10/30/2017		S		10(1)	D	\$56.75	130,440	I	By Family Partnership	
Common Stock					10/31/2017		S		12,200(1)	D	\$55.62(6)	3,120,255	D		
Common Stock					10/31/2017		S		6,700(1)	D	\$56.23 ⁽⁷⁾	3,113,555	D		
Common Stock					10/31/2017		S		418(1)	D	\$55.95	130,022	I	By Family Partnership	
Common Stock												20,000	I	By Spouse	
Common Stock												60,946	I	See footnote ⁽⁸⁾	
							. ,	•	sed of, or Benef	•	ned				
1. Title of Derivative Security (Instr. 3)	Conversion		3A. Deemed Execution Date, if any	4. Transactio (Instr. 8)	on Code 5. Nu	mber of Derivative rities Acquired (A) o osed of (D) (Instr. 3	6. Date	e Exercis	sable and 7. Title are		Securities Underly rr. 3 and 4)	ying 8. Price of Derivative Security (Instr. Secu	ative Form: Direct	11. Nature of Indirect Beneficial	

Price of Derivative		(Month/Day/Year)			4 and 5)					5)	Beneficially Owned	(I) (Instr. 4)	Ownership (Instr.
Security									Amount or		Following Reported		7'
			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Number of Shares		Transaction(s)		

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$55.25 to \$56.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$56.25 to \$57.225. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$57.25 to \$57.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$55.65 to \$56.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$55.10 to \$56.075. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$56.10 to \$56.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

Date

11/01/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep $\underline{NeffThomas\ B}$	orting Person [*]						d Ticker or Tra		nbol						5. Relation (Check a	all app	of Reporting I licable) irector	Person(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	1iddle)		3. Date of 11/16/201		Transaction (M	/lonth/Da	y/Year)						X		fficer (give title	e below) Chief Exe	ecutive (Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amen	dment,	Date of Origina	al Filed (Month/[Day/Y	'ear)				6. Indivi		r Joint/Group orm filed by O			•	
(Street) SAN FRANCISCO	CA	94	4158													F	orm filed by M	ore than	One Rep	orting Person	
(City)	(State)	(Z	ip)																		
			Т	able I -	Non-Deriv	ative	Securities	Acquii	red, D	ispo	osed of,	or Bene	eficially O	wned							
1. Title of Security (Instr. 3)					2. Transaction	E	A. Deemed xecution Date,		nsaction (Instr. 8)		4. Securitie (Instr. 3, 4 a		d (A) or Dispo	sed Of	(D)	Bene	nount of Securi		Direct (ership Form: D) or Indirect	7. Nature of Indirect
					(Month/Day/		any //onth/Day/Year)	Code	v		Amount		(A) or (D)	Price			wing Reported action(s) (Instr		(I) (Insti	r. 4)	Beneficial Ownership (Instr. 4)
Common Stock					11/16/20	17		S			4,000	0(1)	D	\$4:	5.62(2)		3,109,555			D	
Common Stock					11/16/20	17		S			11,90	0(1)	D	\$40	5.67(3)		3,097,655			D	
Common Stock					11/16/20	17		S			3,000	0(1)	D	\$4	7.62(4)		3,094,655			D	
Common Stock					11/16/20	17		S			4189	(1)	D	\$40	5.75 ⁽⁵⁾		129,604			I	By Family Partnership
Common Stock					11/17/20	17		S			16,00	00(1)	D	\$4	6.6(6)		3,078,655			D	
Common Stock					11/17/20	17		S			2,900	0(1)	D	\$40	5.98 ⁽⁷⁾		3,075,755			D	
Common Stock					11/17/20	17		S			4189	(1)	D	\$40	5.75(8)		129,186			I	By Family Partnership
Common Stock																	20,000			I	By Spouse
Common Stock																	60,946			I	See footnote ⁽⁹⁾
				Table I			ecurities Ad							ned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative		3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securiti	per of Derivative es Acquired (A) ed of (D) (Instr.	or Exp	Date Exe piration onth/Day	Date	[d Amount of S Security (Inst				8. Price of Derivative Security (Instr 5)	9. Num derivat Securit Benefic	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security	1		l														Follow			l <i>'</i>

- 1			I	1		l			1	Amount or	Reported		1
- 1			l .	1		l	Date	Expiration		Number of	Transaction(s)		1
			Code	V	(A)	(D)			Title	Shares	(Instr. 4)		L

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$45.25 to \$46.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$46.25 to \$47.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$47.375 to \$48.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$46.70 to \$47.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$45.85 to \$46.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$46.825 to \$47.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$46.65 to \$46.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

11/17/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

l	OMB APPROVAL	
	OMB Number:	3235-0287
	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]						and Ticker NINC [1		g Symbol							nip of Reporting Popplicable) Director	erson(s) to	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 12/01/20		st Transac	ction (Mon	th/Day/Ye	ear)						Officer (give title	below)	cutive Of		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	t, Date of 0	Original F	iled (Mon	ith/Day/	Year)			6.		or Joint/Group F Form filed by On				
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	ore than O	ne Repor	ting Person	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	ivativ	e Securi	ities Ac	quired	, Disp	osed of	, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact		2A. Deeme Execution		. Transact Code (Inst		4. Securi (Instr. 3,		d (A) or Dispose	ed Of (D)	Bei	Amount of Securiti	- 1	Direct (D)	ship Form: or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day	ay/Year)	ode	v	Amount		(A) or (D)	Price		lowing Reported nsaction(s) (Instr.		(I) (Instr. 4	1)	Beneficial Ownership (Instr. 4)
Common Stock					12/01/2	017			F		4,6	89(1)	D	\$47.1	5	3,071,066			D	
Common Stock																129,186			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽²⁾
				Table I					,	•	,	or Benefi e securit	cially Owneries)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Secur	mber of Der rities Acquir osed of (D) (5)	ired (A) or	6. Date Expirati (Month/	ion Date			d Amount of Sec Security (Instr.		iderlying	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficia	re F	0. Ownership orm: Direct D) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	D)	Date Exercis		Expiration Date	Title		Amount Numbe Shares			Owned Followin Reported Transacti (Instr. 4)	d tion(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/05/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]						ind Ticker o	,	g Symbol							hip of Reporting P pplicable)	erson(s) t	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/06/20		st Transact	tion (Mont	h/Day/Yea	r)					X	Officer (give title	below)	cutive O		ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	t, Date of C	Original F	iled (Month	n/Day/`	Year)			6.	Individua X	l or Joint/Group F Form filed by Or				
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	ore than C	ne Repo	orting Person	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	ivativ	e Securi	ities Ac	quired,	Disp	osed of	, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact Date		2A. Deemed Execution		. Transactio		4. Securit (Instr. 3,		d (A) or Dispose	ed Of (D)	Be	Amount of Securiti		Direct (D	rship Form: 0) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day		if any (Month/Day	y/Year)	ode \	,	Amount		(A) or (D)	Price		llowing Reported ansaction(s) (Instr.		(I) (Instr.	4)	Ownership (Instr. 4)
Common Stock					12/06/20	017			F		3,2	61(1)	D	\$44.8	35	3,067,805			D	
Common Stock																129,186			I	By Family Partnership
Common Stock																20,000			I	By Spouse
Common Stock																60,946			I	See footnote ⁽²⁾
				Table I			Securitie calls, wa		,	•	,		cially Owne ies)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Secur	mber of Der rities Acquir osed of (D) (5)	red (A) or	6. Date E Expiratio (Month/D	n Date	.		d Amount of Sec Security (Instr.		nderlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici	/e es	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)))	Date Exercisal		xpiration ate	Title		Amour Numbe Shares	er of		Owned Followin Reporte Transact (Instr. 4)	d tion(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/08/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Re	porting Person*			and Ticker or Trace Name 1		ol			(Check	tionship of Reporting Person(s all applicable)	•	
	(First)	(Middle)	3. Date of Earlie 12/14/2017	est Transaction (M	lonth/Day/\	rear)			X		10% Ow Other (s	vner specify below)
(Last) C/O FIBROGEN, INC.	(FIRST)	(Middle)								Chief Ex	ecutive Officer	
409 ILLINOIS ST.			4. If Amendmen	nt, Date of Origina	al Filed (Mo	onth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C		
(Street)			•							Form filed by More than	•	
SAN FRANCISCO	CA	94158										
(City)	(State)	(Zip)										
		Table I -	Non-Derivativ	e Securities	Acquire	d, Disp	oosed of, or Ben	eficially C	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect Beneficial
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Ownership (Instr.
Common Stock			12/14/2017		S		6,918(1)	D	\$42.18 ⁽²⁾	3,060,887	D	
Common Stock			12/14/2017		S		11,782(1)	D	\$43.01 ⁽³⁾	3,049,105	D	
Common Stock			12/14/2017		S		200(1)	D	\$43.6	3,048,905	D	
Common Stock			12/14/2017		S		360(1)	D	\$42.09(4)	128,826	I	By Family Partnership
Common Stock			12/14/2017		S		58(1)	D	\$43.08(5)	128,768	I	By Family Partnership
Common Stock			12/15/2017		S		10,552(1)	D	\$41.37(6)	3,038,353	D	
Common Stock			12/15/2017		S		8,048(1)	D	\$42.07(7)	3,030,305	D	
Common Stock			12/15/2017		S		300(1)	D	\$42.78(8)	3,030,005	D	
Common Stock			12/15/2017		S		418(1)	D	\$41.49(9)	128,350	I	By Family Partnership
Common Stock										20,000	I	By Spouse
Common Stock										60,946	I	See footnote ⁽¹⁰⁾
		Table	II - Derivative	Securities Ac	quired,	Dispo	sed of, or Benef	icially Ow	ned			footnote ⁽¹

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)		5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Yo	ite	7. Title and Amount of Secu Derivative Security (Instr. 3		Derivative Security (Instr.	derivative Securities	(D) or Indirect	Indirect
	Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Following Reported Transaction(s) (Instr. 4)		4)

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$41.60 to \$42.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$42.60 to \$43.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$41.90 to \$42.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$42.95 to \$43.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$40.75 to \$41.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$41.725 to \$42.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$42.75 to \$42.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$41.20 to \$41.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

Date

12/15/2017

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person*		<u>FIBROGE</u>	and Ticker or Trace N INC [FGEN]				5. Rela (Check	tionship of Reporting Person(s all applicable) Director) to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 12/20/2017	est Transaction (M	onth/Day/Y	ear)			X	,	Other (specutive Officer	pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Tab	le I - Non-Derivati	e Securities	Acquire	l, Disp	oosed of, or Ber	eficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	esed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect Beneficial
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Ownership (Instr.
Common Stock			12/20/2017		S		7,071(1)	D	\$43.66 ⁽²⁾	3,022,934	D	
Common Stock			12/20/2017		S		11,829(1)	D	\$44.39(3)	3,011,105	D	
Common Stock			12/20/2017		S		418(1)	D	\$43.64 ⁽⁴⁾	127,932	I	By Family Partnership
Common Stock			12/21/2017		М		24,541	A	\$3.6	3,035,646	D	
Common Stock			12/21/2017		М		36,735	A	\$2.9	3,072,381	D	
Common Stock			12/21/2017		M		18,724	A	\$3.5	3,091,105	D	
Common Stock			12/21/2017		S		9,377(1)	D	\$44.92 ⁽⁵⁾	3,081,728	D	
Common Stock			12/21/2017		S		9,523(1)	D	\$45.52(6)	3,072,205	D	
Common Stock			12/21/2017		S		418(1)	D	\$45.22 ⁽⁷⁾	127,514	I	By Family Partnership
Common Stock										20,000	I	By Spouse
Common Stock										60,946	I	See footnote ⁽⁸⁾
		Ta	able II - Derivative (e.g., puts				sed of, or Benef onvertible securi		ned			
1. Title of Derivative Security (Instr. 3)	2. Conversion			umber of Derivative				nd Amount of S e Security (Ins	Securities Underl r. 3 and 4)	ying 8. Price of 9. Nur Derivative deriva		11. Nature of Indirect

	Price of	(Month/Day/Year)	if any (Month/Day/Year)			Disposed of 4 and 5)	(D) (Instr. 3,	(Month/Day/Y	ear)			Security (Instr. 5)	Beneficially	(D) or Indirect (I) (Instr. 4)	Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	12/21/2017		М			24,541	(9)	03/11/2019	Common Stock	24,541	\$0.00	0	D	
Stock Option (Right to Buy)	\$2.9	12/21/2017		M			36,735	(9)	06/09/2020	Common Stock	36,735	\$0.00	0	D	
Stock Option (Right to Buy)	\$3.5	12/21/2017		М			18,724	(9)	06/07/2021	Common Stock	18,724	\$0.00	32,870	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$43.15 to \$44.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$44.15 to \$44.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$43.35 to \$44.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$44.35 to \$45.325. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$45.35 to \$45.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$45.10 to \$45.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/22/2017

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person*					e and Ticker or Trac N INC [FGEN	0 ,	ol					tionship of Reporting all applicable) Director	Person(s) t	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of Ear 12/28/2017	liest Transaction (M	onth/Day/\	rear)				X	Officer (give ti	le below) Chief Exe	cutive O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amendme	ent, Date of Origina	l Filed (Mo	onth/Day	/Year)			6. Indiv	idual or Joint/Group Form filed by 0	• •		,	
(Street) SAN FRANCISCO	CA	94	158										Form filed by I	More than (One Repo	orting Person	
(City)	(State)	(Z	p)														
			Т	able I -	Non-Derivat	ive Securities	Acquire	d, Disp	oosed of,	or Bene	eficially O	wned					
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Year		3. Transa Code (Ins		4. Securities (Instr. 3, 4 a		d (A) or Dispo	sed Of (D)	5. Amount of Secur Beneficially Owned Following Reporte	ı		rship Form: i) or Indirect 4)	7. Nature of Indirect Beneficial
					, , , , ,	(Month/Day/Year)	Code	v	Amount		(A) or (D)	Price	Transaction(s) (Ins. 4)		()(,	Ownership (Instr. 4)
Common Stock					12/15/2017		G	v	500	0	D	\$0.00	3,071,70	5		D	
Common Stock					12/15/2017		G	v	500	0	D	\$0.00	19,500			I	By Spouse
Common Stock					12/28/2017		S		18,55	50(1)	D	\$48.28(2)	3,053,15	5		D	
Common Stock					12/28/2017		S		3500	(1)	D	\$48.72(3)	3,052,80	5		D	
Common Stock					12/28/2017		S		4180	(1)	D	\$48.3(4)	127,096			I	By Family Partnership
Common Stock					12/29/2017		S		9,087	7 ⁽¹⁾	D	\$48.06(5)	3,043,71	3		D	
Common Stock					12/29/2017		S		9,813	3(1)	D	\$48.88(6)	3,033,90	5		D	
Common Stock					12/29/2017		S		4180	(1)	D	\$48.36 ⁽⁷⁾	126,678			I	By Family Partnership
Common Stock													60,946			I	See footnote ⁽⁸⁾
				Table I		Securities Ac s, calls, warran						ned					
Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative		3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	action Code 5. N	lumber of Derivative curities Acquired (A) posed of (D) (Instr. 3 and 5)	6. Dat		sable and 7	7. Title and	-	ecurities Underly r. 3 and 4)	8. Price of Derivative Security (Inst	9. Numb derivativ r. Securiti Benefic Owned	ve lies (10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Security	1	[T	Т					Followi	ng]"

- 1				I	I					Amount or	Reported		i
- 1				l	l		Date	Expiration		Number of	Transaction(s)		i
- 1			Code	v	(A)	(D)		Date	Title	Shares	(Instr. 4)		i

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$47.70 to \$48.675. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$48.70 to \$48.725. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$48.00 to \$48.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$47.45 to \$48.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$48.45 to \$49.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$47.45 to \$48.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

01/02/2018

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person*					and Ticker or Trac <u>VINC</u> [FGEN		ol				ionship of Reporting Pera all applicable) Director	son(s) to Issu	er 10% Owi	ner
(Last) C/O FIBROGEN, INC.	(First)	(N	Middle)		3. Date of Earlie 01/04/2018	est Transaction (M	onth/Day/\	′ear)			X	Officer (give title be	elow) of Executive	Other (sp	pecify below)
409 ILLINOIS ST.					4. If Amendme	nt, Date of Origina	l Filed (Mo	onth/Day	Year)		6. Indivi	dual or Joint/Group Filin Form filed by One			
(Street) SAN FRANCISCO	CA	92	4158									Form filed by More	than One Re	porting Person	
(City)	(State)	(Z	(ip)												
			7	Γable I -	Non-Derivativ	e Securities	Acquire	d, Disp	osed of, or Ber	neficially O	wned				
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported		nership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day/rear)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3		u. +)	Ownership (Instr 4)
Common Stock					01/04/2018		S		4,018(1)	D	\$47.92 ⁽²⁾	3,029,887		D	
Common Stock					01/04/2018		S		13,082(1)	D	\$49.04 ⁽³⁾	3,016,805		D	
Common Stock					01/04/2018		S		1,800(1)	D	\$49.7(4)	3,015,005		D	
Common Stock					01/04/2018		S		418(1)	D	\$48.89 ⁽⁵⁾	126,260		I	By Family Partnership
Common Stock					01/05/2018		S		10,800(1)	D	\$45.84 ⁽⁶⁾	3,004,205		D	
Common Stock					01/05/2018		S		6,698(1)	D	\$46.97 ⁽⁷⁾	2,997,507		D	
Common Stock					01/05/2018		S		1,402(1)	D	\$47.6 ⁽⁸⁾	2,996,105		D	
Common Stock					01/05/2018		S		418(1)	D	\$45.84 ⁽⁹⁾	125,842		I	By Family Partnership
Common Stock												60,946		I	See footnote ⁽¹⁰⁾
Common Stock												19,500		Ι	By Spouse
				Table I					sed of, or Bene nvertible secur		ned				
1. Title of Derivative Security (Instr. 3)	Conversion	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any	4. Transa (Instr. 8)	Secu	umber of Derivative rities Acquired (A) osed of (D) (Instr. 3	or Expira	ation Dat	e Derivativ	nd Amount of S e Security (Inst	ecurities Underly r. 3 and 4)		. Number of lerivative securities	10. Ownership Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial

	Price	ce of	(Month/Day/Year)			4 and 5)						5)	Beneficially Owned	(I) (Instr. 4)	Ownership (Instr.
- 1	Secu												Following		4)
- 1		,									Amount or		Reported		
- 1		- 1						Date	Expiration		Number of	l	Transaction(s)		
- 1				Code	V	(A)	(D)	Exercisable	Date	Title	Shares		(Instr. 4)		

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$47.50 to \$48.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$48.55 to \$49,525. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 4. The shares were sold at prices ranging from \$49.55 to \$50.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$48.65 to \$49.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$45.50 to \$46.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$46.50 to \$47.475. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$47.525 to \$47.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$45.60 to \$45.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

Date

01/08/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	rting Person [*]						nd Ticker or Tr INC [FGEN		Symbol							onship of Repor all applicable) Director	ting Pers	son(s) to	Issuer	10% Own	or.
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o		t Transaction (Month/I	Day/Ye	ar)					X	Officer (giv		•	utive Offi	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	endment,	, Date of Origin	al File	d (Mon	th/Day	(Year)				6. Indivi	dual or Joint/Gr Form filed				ble Line)	
(Street) SAN FRANCISCO	CA	94	158													Form filed	-	-	-	ing Person	
(City)	(State)	(Zi	p)																		
			7	able I -	Non-Der	ivative	Securities	Acqı	uired,	, Disp	osed of	f, or Ben	eficially C	wned							
1. Title of Security (Instr. 3)					2. Transact		2A. Deemed Execution Date		ransact le (Instr		4. Securi (Instr. 3,		ed (A) or Disp	osed Of	(D)	5. Amount of Se Beneficially Ov	ned	0		or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day/Yea	Cod	de	v	Amount		(A) or (D)	Price		Following Rep Transaction(s) 4)			(I) (Instr. 4)		Beneficial Ownership (Instr. 4)
Common Stock					01/18/2	018		Т	S		14,	658(1)	D	\$4	7.56(2)	2,981	,447]	D	
Common Stock					01/18/2	018			S		4,2	242(1)	D	\$4	7.92(3)	2,977	,205]	D	
Common Stock					01/18/2	018			S		41	18(1)	D	\$4	7.51 ⁽⁴⁾	125,4	424			I	By Family Partnership
Common Stock					01/19/2	018			S		15,	200(1)	D	\$4	7.18 ⁽⁵⁾	2,962	,005]	D	
Common Stock					01/19/2	018			S		3,7	700(1)	D	\$4	7.68(6)	2,958	,305]	D	
Common Stock					01/19/2	018			S		41	18(1)	D	\$4	7.11 ⁽⁷⁾	125,0	006			I	By Family Partnership
Common Stock																60,9	46			I	See footnote ⁽⁸⁾
Common Stock																19,5	000			I	By Spouse
				Table I			ecurities A							ned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	Securit	nber of Derivati ties Acquired (A sed of (D) (Instr 5)) or E	6. Date Expirati (Month/I	ion Dat			d Amount of			8. Price of Derivative Security (5)	d Instr. S	D. Numbe derivative Securities Beneficia Dwned	e Fo	. Ownership rm: Direct) or Indirect (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Nu	nount or mber of ares		F R T	Following Reported Fransaction Instr. 4)	ĭ		,

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$46.90 to \$47.875. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$47.90 to \$48.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$47.30 to \$47.675. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$46.55 to \$47.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$47.55 to \$47.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$46.70 to \$47.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks

/s/ Dorothy Pacini, Attorney-in-fact

Date

01/19/2018

** Signature of Reporting Person

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person [*]		I	and Ticker or Trace In the Indiana Trace In the Indiana Trace In the Indiana I		ol				tionship of Reporting Person(s all applicable) Director) to Issuer 10% Ow	upor.
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earlie 01/29/2018	est Transaction (M	onth/Day/Y	ear)			X	Officer (give title below)		specify below)
409 ILLINOIS ST.			4. If Amendmen	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C Form filed by One Repo		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Tal	ble I - Non-Derivativ	e Securities	Acquire	d, Dis	oosed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
			(MOIIII/Day/Teal)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (111511.4)	Ownership (Insti
Common Stock			01/29/2018		S		200(1)	D	\$59.3(2)	2,958,105	D	
Common Stock			01/29/2018		S		4,500(1)	D	\$61.06 ⁽³⁾	2,953,605	D	
Common Stock			01/29/2018		S		13,800(1)	D	\$61.82 ⁽⁴⁾	2,939,805	D	
Common Stock			01/29/2018		S		400(1)	D	\$62.43(5)	2,939,405	D	
Common Stock			01/29/2018		S		418(1)	D	\$61.64(6)	124,588	I	By Family Partnership
Common Stock			01/30/2018		S		10,000(1)	D	\$60.81 ⁽⁷⁾	2,929,405	D	
Common Stock			01/30/2018		S		8,700(1)	D	\$61.54 ⁽⁸⁾	2,920,705	D	
Common Stock			01/30/2018		S		200(1)	D	\$62.49(9)	2,920,505	D	
Common Stock			01/30/2018		S		418(1)	D	\$61.28(10)	124,170	I	By Family Partnership
Common Stock										60,946	I	See footnote ⁽¹¹⁾
										19,500	ī	By Spouse

	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	Execution Date,			5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Da (Month/Day/Y	ite	7. Title and Amount of Secu Derivative Security (Instr. 3	and 4)	8. Price of Derivative Security (Instr. 5)	derivative	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Following Reported Transaction(s) (Instr. 4)		4)

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$59.00 to \$59.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$60.375 to \$61.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$61.375 to \$62.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$62.375 to \$62.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 6. The shares were sold at prices ranging from \$61.50 to \$61.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$60.25 to \$61.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices tanging from 900.25 to 901.20. The reporting person with provide upon request to the 152c, the issuer of security notice of the issuer, that information regulating the number of shares sold at each separate prices.
- 8. The shares were sold at prices ranging from \$61.25 to \$62.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 9. The shares were sold at prices ranging from \$62.40 to \$62.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares were sold at prices ranging from \$60.75 to \$61.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 11. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

01/31/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B (Last)	eporting Person* (First)	(Middle)	FIBROGE	and Ticker or Trace N INC FGEN est Transaction (M]					Officer (give title below)	10% Ow	ner pecify below)
C/O FIBROGEN, INC. 409 ILLINOIS ST. (Street)			4. If Amendme	nt, Date of Origina	al Filed (Mo	onth/Day	Year)		6. Indiv	idual or Joint/Group Filing (Cl Form filed by One Repo Form filed by More than	rting Person	
SAN FRANCISCO (City)	CA (State)	94158 (Zip)	_									
		Table	I - Non-Derivati	ve Securities	Acquire	d, Disp	osed of, or Ben	eficially O	wned			
1. Title of Security (Instr. 3	;)		2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
			(,	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(,, (,	Ownership (Instr.
Common Stock			02/22/2018		М		10,265	A	\$2.35	2,955,614	D	
Common Stock			02/22/2018		S		8,749(1)	D	\$56.5 ⁽²⁾	2,946,865	D	
Common Stock			02/22/2018		S		10,051(1)	D	\$57.43(3)	2,936,814	D	
Common Stock			02/22/2018		S		100(1)	D	\$58.025	2,936,714	D	
Common Stock			02/22/2018		S		618(1)	D	\$56.5 ⁽⁴⁾	123,552	I	By Family Partnership
Common Stock			02/22/2018		S		300(1)	D	\$57.72 ⁽⁵⁾	123,252	I	By Family Partnership
Common Stock			02/23/2018		М		10,265	A	\$2.35	2,946,979	D	
Common Stock			02/23/2018		S		11,400(1)	D	\$55.9(6)	2,935,579	D	
Common Stock			02/23/2018		S		6,500(1)	D	\$56.89(7)	2,929,079	D	
Common Stock			02/23/2018		S		1,000(1)	D	\$57.4 ⁽⁸⁾	2,928,079	D	
Common Stock			02/23/2018		S		500(1)	D	\$55.79 ⁽⁹⁾	122,752	I	By Family Partnership
Common Stock			02/23/2018		S		418(1)	D	\$57.11(10)	122,334	I	By Family Partnership
				1		$\overline{}$	1	Ť T		1	1	

			Т	able I -	Non-Deri	ative S	ecurities A	cquired,	Dispos	sed of	, or Beneficially O	wned				
1. Title of Security (Instr. 3)					2. Transacti Date	Exe	Deemed cution Date,	3. Transaction Code (Instr.		l. Securit Instr. 3, 4	ties Acquired (A) or Dispo 4 and 5)		5. Amount of Securit Beneficially Owned	Direc	nership Form: t (D) or Indirect	7. Nature of Indirect
					(Month/Day/	Year) if an (Moi	nth/Day/Year)	Code	/ A	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 4)		str. 4)	Beneficial Ownership (Inst 4)
Common Stock													19,500		Ι	By spouse
Common Stock													60,946		I	See footnote ⁽¹¹⁾
				Table I				•	•		or Beneficially Owr e securities)	ned				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)		Securities	of Derivative Acquired (A) of (D) (Instr. 3	or Expiration			7. Title and Amount of S Derivative Security (Inst		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Inst
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		piration te	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.35	02/22/2018		М			10,265	(12)	03/1	12/2018	Common Stock	10,265	\$0.00	27,535	D	
	\$2.35	02/23/2018	1	1			10,265	(12)	03/1			10,265	\$0.00	17,270		

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$56.00 to \$56.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$57.00 to \$57.925. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$56.125 to \$57.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$57.60 to \$57.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$55.35 to \$56.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$56.35 to \$57.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$57.35 to \$57.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 9. The shares were sold at prices ranging from \$55.45 to \$56.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares were sold at prices ranging from \$56.725 to \$57.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 11. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 12. Fully vested

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

02/23/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	rting Person [*]						d Ticker or Tra	_	Symbol						nship of Reportin I applicable) Director	Person(s) to Issue	r 10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/01/20		Transaction (I	Month/	'Day/Year)					X	Officer (give) xecutive (ecify below)
409 ILLINOIS ST.					4. If Ame	ndment,	Date of Origin	al File	ed (Month/Da	ay/Year)				6. Individu	ual or Joint/Grou Form filed by	• •		,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by	More tha	n One Rep	porting Person	
(City)	(State)	(Zi	p)																
			Т	able I -	Non-Deri	ivative	Securities	Acq	uired, Di	spose	d of, or B	eneficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact Date	E	A. Deemed Execution Date,		ransaction de (Instr. 8)		ecurities Acq tr. 3, 4 and 5)	uired (A) or Dispos	ed Of ([:	5. Amount of Sec Beneficially Own	d	Direct	ership Form: (D) or Indirect	7. Nature of Indirect
					(Month/Day		f any Month/Day/Year	Co.	de V	Amo	ount	(A) or (D)	Price	·	Following Repor Transaction(s) (In 4)		(I) (Inst	tr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					03/01/20	018			F		4,455(1)	D	\$5	4.95	2,923,6	.4		D	
Common Stock															122,33	1		I	By Family Partnership
Common Stock															19,500			I	By Spouse
Common Stock															60,946			I	See footnote ⁽²⁾
				Table I			ecurities A alls, warra	•			•	eficially Own	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securit	ber of Derivativies Acquired (A ed of (D) (Instr.)	or	6. Date Exer Expiration D (Month/Day/	ate		and Amount of Se ive Security (Instr.			8. Price of Derivative Security (In: 5)	tr. Secu Bene	rities ficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisable	Expira Date	ition Title			ount or ober of res		Owner Follo Repo Trans (Instr	wing rted action(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/05/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep	porting Person*			and Ticker or Trac		ol			(Check	tionship of Reporting Person(s all applicable)		
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 03/06/2018	est Transaction (M	onth/Day/Y	'ear)			X	Officer (give title below)	10% Ow Other (s ecutive Officer	ner pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	onth/Day	'/Year)		6. Indiv		rting Person	
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Table	I - Non-Derivati	ve Securities	Acquire	d, Disp	posed of, or Ben	eficially O	vned			
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
			(monumbay/real)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (111341. 4)	Ownership (Instr.
Common Stock			03/06/2018		F		16,199(1)	D	\$53.55	2,907,425	D	
Common Stock			03/07/2018		М		10,265	A	\$2.35	2,917,690	D	
Common Stock			03/07/2018		S		8,802(2)	D	\$52.58 ⁽³⁾	2,908,888	D	
Common Stock			03/07/2018		S		7,800(2)	D	\$53.26 ⁽⁴⁾	2,901,088	D	
Common Stock			03/07/2018		S		2,298(2)	D	\$54.14 ⁽⁵⁾	2,898,790	D	
Common Stock			03/07/2018		S		700(2)	D	\$52.82 ⁽⁶⁾	121,634	I	By Family Partnership
Common Stock			03/07/2018		S		218(2)	D	\$53.91 ⁽⁷⁾	121,416	I	By Family Partnership
Common Stock			03/08/2018		М		7,005	A	\$2.35	2,905,795	D	
Common Stock			03/08/2018		M		3,314	A	\$3.6	2,909,109	D	
Common Stock			03/08/2018		S		6,400(2)	D	\$52.74(8)	2,902,709	D	
Common Stock			03/08/2018		S		11,800(2)	D	\$53.44 ⁽⁹⁾	2,890,909	D	
Common Stock			03/08/2018		S		700(2)	D	\$54.09(10)	2,890,209	D	
Common Stock			03/08/2018		S		300(2)	D	\$52.55(11)	121,116	I	By Family Partnership

1. Title of Security (Instr. 3)	2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	d (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
	(Month/Day/Year)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Inst 4)
Common Stock	03/08/2018		S		618(2)	D	\$53.59(12)	120,498	I	By Family Partnership
Common Stock								19,500	I	By Spouse
Common Stock								60,946	I	See footnote ⁽¹³⁾

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	Conversion or Exercise (Month/Day/Ye		3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		Derivative Security (Instr.	derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.35	03/07/2018		M			10,265	(14)	03/12/2018	Common Stock	10,265	\$0.00	7,005	D	
Stock Option (Right to Buy)	\$2.35	03/08/2018		M			7,005	(14)	03/12/2018	Common Stock	7,005	\$0.00	0	D	
Stock Option (Right to Buy)	\$3.6	03/08/2018		M			3,314	(14)	03/11/2019	Common Stock	3,314	\$0.00	472,145	D	

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Shares sold pursuant to a 10b5-1 plan.
- 3. The shares were sold at prices ranging from \$52.00 to \$52.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$53.00 to \$53.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$54.00 to \$54.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$52.30 to \$53.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$53.55 to \$54.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$52.05 to \$53.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$53.05 to \$53.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares were sold at prices ranging from \$54.00 to \$54.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 11. The shares were sold at prices ranging from \$52.05 to \$52.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 12. The shares were sold at prices ranging from \$53.20 to \$54.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 13. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 14. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

03/08/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person*					e and Ticker or Trac EN INC [FGEN	0 ,	ol				tionship of Reporting Pers all applicable) Director	son(s) to Issuer	10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	liddle)		3. Date of Ear 03/20/2018	liest Transaction (M	onth/Day/\	Year)			X	Officer (give title be	elow) of Executive C	Other (sp	pecify below)
409 ILLINOIS ST.					4. If Amendm	ent, Date of Origina	l Filed (Mo	onth/Day	Year)		6. Indiv	ridual or Joint/Group Filin	•	,	
(Street) SAN FRANCISCO	CA	94	158									Form filed by More	than One Rep	orting Person	
(City)	(State)	(Zi	ip)												
			T	able I - I	Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned										
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Yea		3. Transa Code (In:		4. Securities Ad (Instr. 3, 4 and	cquired (A) or Dispo 5)	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					((Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 a		,	Ownership (Instr. 4)
Common Stock					03/20/2018		М		9,042	A	\$3.6	2,969,251		D	
Common Stock					03/20/2018		S		14,932(1)	D	\$50.64(2)	2,954,319		D	
Common Stock					03/20/2018		S		3,968(1)	D	\$51.02 ⁽³⁾	2,950,351		D	
Common Stock					03/20/2018		S		918(1)	D	\$50.71 ⁽⁴⁾	119,580		I	By Family Partnership
Common Stock					03/21/2018		М		9,042	A	\$3.6	2,959,393		D	
Common Stock					03/21/2018		S		18,000(1)	D	\$51.17 ⁽⁵⁾	2,941,393		D	
Common Stock					03/21/2018		S		900(1)	D	\$51.63 ⁽⁶⁾	2,940,493		D	
Common Stock					03/21/2018		S		918(1)	D	\$51.13 ⁽⁷⁾	118,662		D	
Common Stock												19,500		I	By Spouse
Common Stock												60,946		I	See footnote ⁽⁸⁾
				Table I					Acquired, Disposed of, or Beneficially rants, options, convertible securities)						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	Se Dis	Number of Derivative curities Acquired (A) sposed of (D) (Instr. 3 and 5)	or Expir	te Exercis ation Dat h/Day/Ye	e Deriv	tle and Amount of S vative Security (Inst		Derivative d Security (Instr. S 5) B	erivative ecurities	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)

	Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Following Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$3.6	03/20/2018	M			9,042	(9)	03/11/2019	Common Stock	9,042	\$0.00	463,103	D	
Stock Option (Right to Buy)	\$3.6	03/21/2018	М			9,042	(9)	03/11/2019	Common Stock	9,042	\$0.00	454,061	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$50.10 to \$50.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$51.00 to \$51.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$50.20 to \$50.875. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$50.575 to \$51.55. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$51.60 to \$51.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$50.65 to \$51.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/22/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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OMB Number:	3235-0287
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hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person [*]			and Ticker or Trac <u>VINC</u> [FGEN		ol				tionship of Reporting Person(s all applicable) Director) to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 04/04/2018	est Transaction (M	onth/Day/Y	'ear)			X	Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C Form filed by One Repo		
(Street) SAN FRANCISCO	CA	94158	-							Form filed by More than	•	
(City)	(State)	(Zip)										
		Table I	- Non-Derivativ	ve Securities A	Acquire	d, Disp	oosed of, or Ben	eficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date		3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	d (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			04/04/2018		M		10,320	A	\$3.6	2,950,813	D	
Common Stock			04/04/2018		S		10,100(1)	D	\$45.16 ⁽²⁾	2,940,713	D	
Common Stock			04/04/2018		S		7,800(1)	D	\$45.97 ⁽³⁾	2,932,913	D	
Common Stock			04/04/2018		S		1,000(1)	D	\$46.68(4)	2,931,913	D	
Common Stock			04/04/2018		S		700(1)	D	\$45.36 ⁽⁵⁾	117,962	I	By Family Partnership
Common Stock			04/04/2018		S		218(1)	D	\$46.59 ⁽⁶⁾	117,744	I	By Family Partnership
Common Stock			04/05/2018		M		10,320	A	\$3.6	2,942,233	D	
Common Stock			04/05/2018		S		10,500(1)	D	\$45.13 ⁽⁷⁾	2,931,733	D	
Common Stock			04/05/2018		S		8,400(1)	D	\$46.2 ⁽⁸⁾	2,923,333	D	
Common Stock			04/05/2018		S		618(1)	D	\$45.06 ⁽⁹⁾	117,126	I	By Family Partnership
Common Stock			04/05/2018		S		300(1)	D	\$46.1(10)	116,826	I	By Family Partnership
Common Stock										19,500	I	By Spouse

Common Steel				Date		(Month/Day/Year) if any		3. Transaction Code (Instr. 8)					Beneficially Owned	Direct (I) (Ins	(D) or Indirect	7. Nature of Indirect Beneficial
G							h/Day/Vaan	Code	v	Amount	(A) or (D)		following Reported Transaction(s) (Instr.)		str. 4)	Ownership (Instr 4)
Common Stock													60,946		I	See footnote ⁽¹¹⁾
				Table I				•			r Beneficially Own e securities)	ed				
(e.g., puts, calls, warrants, options, convertible securities) 1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of Obsposed of (D) (Instr. 3, 4 and 5) 2. Tansaction Date Execution Date (Instr. 8) 3. Transaction Date (Instr. 8) 4. Transaction Code (Instr. 8) 5. Number of Derivative Security (Instr. 3 and 4) 5. Det Exercisable and Expiration Date (Month/Day/Year) 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) 8. Price of Derivative Security (Instr. 3 and 4) 9. Number of derivative Security (Instr. 3 and 4) 9. Number of derivative Security (Instr. 3 and 4) 9. Number of derivative Security (Instr. 3 and 4) 10. Ownership (Indirect Security (Instr. 3 and 4)) 11. Nature of Derivative Security (Instr. 3 and 4) 12. Derivative Security (Instr. 3 and 4) 13. Transaction Date (Instr. 8) 14. Transaction Date (Instr. 8) 15. Derivative Security (Instr. 3 and 4) 16. Date Exercisable and Expiration Date (Month/Day/Year) 17. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) 18. Price of Derivative Security (Instr. 3 and 4) 19. Number of derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and 4) 19. Number of Derivative Security (Instr. 3 and													Indirect			
	Derivative Security			Code V (A) (D) Exercisable Date Expiration Date Title Shares Owned Following Reported Transaction(s) (Instr. 4)							4)					
Stock Option (Right to Buy)	\$3.6	04/04/2018		М			10,320	(12)	03	3/11/2019	Common Stock	10,320	\$0.00	443,741	D	

03/11/2019

Common Stock

10.320

Stock Option (Right to Buy) Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$44.55 to \$45.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 3. The shares were sold at prices ranging from \$45.55 to \$46.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$46.55 to \$46.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$45.00 to \$45.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 6. The shares were sold at prices ranging from \$46.40 to \$46.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$45.00 to \$45.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$46.05 to \$46.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 9. The shares were sold at prices ranging from \$45.00 to \$45.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares were sold at prices ranging from \$46.10 to \$46.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 11. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

M

12. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

10 320

Date

04/06/2018

433.421

D

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

04/05/2018

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^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

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STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person*					e and Ticker or Trac N INC [FGEN		ol				iionship of Reporting Persor all applicable) Director	(s) to Issuer	vner
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of Ear 04/17/2018	liest Transaction (M	onth/Day/\	′ear)			X	Officer (give title belo		specify below)
409 ILLINOIS ST.					4. If Amendm	ent, Date of Origina	l Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filing Form filed by One Re	, ,	
(Street) SAN FRANCISCO	CA	94	158									Form filed by More th	an One Reporting Persor	
(City)	(State)	(Zi	p)											
			Т	able I - I	Non-Derivat	ive Securities A	Acquire	d, Disp	oosed of, or Be	neficially C	wned			
1. Title of Security (Instr. 3)				- 1	2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acqu (Instr. 3, 4 and 5)	ired (A) or Disp	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
					(Month/Day/Yea) if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(i) (instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					04/17/2018		M		10,320	A	\$3.6	2,933,653	D	
Common Stock					04/17/2018		S		5,200(1)	D	\$47.94 ⁽²⁾	2,928,453	D	
Common Stock					04/17/2018		S		13,700(1)	D	\$48.59 ⁽³⁾	2,914,753	D	
Common Stock					04/17/2018		S		918(1)	D	\$48.54 ⁽⁴⁾	115,908	I	By Family Partnership
Common Stock					04/18/2018		M		10,320	A	\$3.6	2,925,073	D	
Common Stock					04/18/2018		S		18,100(1)	D	\$48.68(5)	2,906,973	D	
Common Stock					04/18/2018		S		800(1)	D	\$49.22(6)	2,906,173	D	
Common Stock					04/18/2018		S		918(1)	D	\$48.6 ⁽⁷⁾	114,990	I	By Family Partnership
Common Stock												19,500	I	By Spouse
Common Stock										60,946	I	See footnote ⁽⁸⁾		
				Table II					sed of, or Beno onvertible secu		ned			
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code 5. Se	Number of Derivative curities Acquired (A) posed of (D) (Instr. 3 nd 5)	rative 6. Date Exercisable (A) or Expiration Date		xercisable and 7. Title and Amount of Securiti n Date Derivative Security (Instr. 3 and			Derivative deri Security (Instr. Sec	umber of vative Form: Direct (D) or Indirect eficially (I) (Instr. 4)	Indirect

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	04/17/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	423,101	D	
Stock Option (Right to Buy)	\$3.6	04/18/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	412,781	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$47.40 to \$48.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 3. The shares were sold at prices ranging from \$48.40 to \$48.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$48.20 to \$48.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$48.15 to \$49.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$49.15 to \$49.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$48.15 to \$49.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

04/18/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

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STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep $\underline{NeffThomas\ B}$	orting Person [*]						d Ticker or Trade NC [FGEN		ool						nship of Reporting Il applicable) Director	Person(s)	to Issue	r 10% Owr	ner	
(Last) C/O FIBROGEN, INC.	(First)	(M	1iddle)		3. Date of 05/02/201		Transaction (M	lonth/Day/	Year)					X	Officer (give tit	le below) Chief Exe	ecutive (Other (sp	ecify below)	
409 ILLINOIS ST.					4. If Amen	dment, I	Date of Origina	al Filed (M	lonth/Day	//Year)				6. Individ	ual or Joint/Group Form filed by 0					
(Street) SAN FRANCISCO	CA	94	¥158												Form filed by I	Nore than	One Rep	oorting Person		
(City)	(State)	(Z	ip)																	
			Т	able I -	Non-Deriv	ative	Securities .	Acquire	d, Dis	posed o	f, or Ben	eficially O	wned							
1. Title of Security (Instr. 3)					2. Transaction	Ex	A. Deemed xecution Date,	3. Transa Code (In			ities Acquired (A) or Disposed Of (I 4 and 5)			·	5. Amount of Securities Beneficially Owned		Direct (ership Form: D) or Indirect	7. Nature of Indirect Beneficial	
					(Month/Day/		any //onth/Day/Year)	Code	v	Amount		(A) or (D)	Price		Following Reporte Transaction(s) (Inst 4)		(I) (Inst	r. 4)	Ownership (Instr.	
Common Stock					05/02/20	18		М		10),320	A	\$.	3.6	2,916,493	3		D		
Common Stock					05/02/20	18		S		18,	,900(1)	D	\$47	.33(2)	2,897,593	3		D		
Common Stock					05/02/20	18		S		9	18(1)	D	\$47	.32(3)	114,072			I	By Family Partnership	
Common Stock					05/03/20	18		М		10),320	A	\$	3.6	2,907,91	3		D		
Common Stock					05/03/20	18		S		16,	,000(1)	D	\$46	.65(4)	2,891,91	3		D		
Common Stock					05/03/20	18		S		2,9	900(1)	D	\$47	7.3 ⁽⁵⁾	2,889,01	3		D		
Common Stock					05/03/20	18		s		9	18(1)	D	\$46	.63(6)	113,154			I	By Family Partnership	
Common Stock															19,500			I	By Spouse	
Common Stock															60,946			I	See footnote ⁽⁷⁾	
				Table I			ecurities Ac alls, warran						ned							
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative		3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securitie	per of Derivative es Acquired (A) ed of (D) (Instr.	or Expir	te Exerci ration Da th/Day/Ye			d Amount of S Security (Inst			8. Price of Derivative Security (Inst	9. Num derivat r. Securit Benefic Owned	ive ties cially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	
	Security	I	1	l											I	Follow			l ´	

			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$3.6	05/02/2018	М			10,320	(8)	03/11/2019	Common Stock	10,320	\$0.00	402,461	D	
Stock Option (Right to Buy)	\$3.6	05/03/2018	М			10,320	(8)	03/11/2019	Common Stock	10,320	\$0.00	392,141	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$46.75 to \$47.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$47.025 to \$47.575. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$46.10 to \$47.075. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$47.10 to \$47.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$46.10 to \$46.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

05/04/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person*			e and Ticker or Trac EN INC [FGEN		ol			(Check	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director 10% Owner				
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of Ear 05/16/2018	liest Transaction (M	onth/Day/\	'ear)			X	Officer (give title belo		specify below)
409 ILLINOIS ST.					4. If Amendm	ent, Date of Origina	l Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filing Form filed by One Re	,	
(Street) SAN FRANCISCO	CA	94	158									Form filed by More th	an One Reporting Person	
(City)	(State)	(Zi	p)											
			Т	able I - N	Non-Derivat	ive Securities A	Acquire	d, Disp	oosed of, or B	eneficially C	wned			
1. Title of Security (Instr. 3)					2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acq (Instr. 3, 4 and 5)	uired (A) or Disp	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
					(Month/Day/Yea	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					05/16/2018		M		10,320	A	\$3.6	2,899,333	D	
Common Stock					05/16/2018		S		9,890(1)	D	\$51.71 ⁽²⁾	2,889,443	D	
Common Stock					05/16/2018		S		9,010(1)	D	\$ 52.29 ⁽³⁾	2,880,433	D	
Common Stock					05/16/2018		S		918(1)	D	\$52.04(4)	112,236	I	By Family Partnership
Common Stock					05/17/2018		М		10,320	A	\$3.6	2,890,753	D	
Common Stock					05/17/2018		S		17,800(1)	D	\$51.62 ⁽⁵⁾	2,872,953	D	
Common Stock					05/17/2018		S		1,100(1)	D	\$52.26(6)	2,871,853	D	
Common Stock					05/17/2018		S		918(1)	D	\$51.62 ⁽⁷⁾	111,318	I	By Family Partnership
Common Stock												19,500	I	By Spouse
Common Stock												60,946	I	See footnote ⁽⁸⁾
				Table II		e Securities Ac s, calls, warran					ned			
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of		3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	Sec Dis	Number of Derivative curities Acquired (A) posed of (D) (Instr. 3 and 5)	or Expira	e Exercis ation Dat h/Day/Ye	te Derivat	and Amount of tive Security (Ins	Securities Underl tr. 3 and 4)	Derivative deri Security (Instr. Sec	umber of vative Form: Direct (D) or Indirect eficially (I) (Instr. 4)	Indirect

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	05/16/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	381,821	D	
Stock Option (Right to Buy)	\$3.6	05/17/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	371,501	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$51.00 to \$51.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 3. The shares were sold at prices ranging from \$52.00 to \$52.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$51.70 to \$52.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$51.15 to \$52.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$52.15 to \$52.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$51.30 to \$52.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

05/18/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep	porting Person*		and Ticker or Trace N INC FGEN		ol		(Check	5. Relationship of Reporting Person(s) to Issuer (Check all applicable)				
, Terr Thornes D			3. Date of Earli	est Transaction (M	onth/Day/Y	ear)			X		10% Ov	
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	06/01/2018	,	,	,			X		Other (s secutive Officer	pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C		
(Street)			_							Form filed by More than	-	
SAN FRANCISCO	CA	94158										
(City)	(State)	(Zip)										
		Table	I - Non-Derivati	ve Securities	Acquire	d, Disp	posed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
			(Month/Day/Tear)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(i) (instr. 4)	Ownership (Instr. 4)
Common Stock			06/01/2018		F		2,287(1)	D	\$54.05	2,869,566	D	
Common Stock			06/04/2018		M		10,320	A	\$3.6	2,879,886	D	
Common Stock			06/04/2018		S		8,730(2)	D	\$54.37(3)	2,871,156	D	
Common Stock			06/04/2018		S		10,170(2)	D	\$54.99(4)	2,860,986	D	
Common Stock			06/04/2018		S		600(2)	D	\$54.58 ⁽⁵⁾	110,718	I	By Family Partnership
Common Stock			06/04/2018		S		318(2)	D	\$55.21(6)	110,400	I	By Family Partnership
Common Stock			06/05/2018		М		10,320	A	\$3.6	2,871,306	D	
Common Stock			06/05/2018		S		16,200(2)	D	\$54.93(7)	2,855,106	D	
Common Stock			06/05/2018		S		2,700(2)	D	\$55.59(8)	2,852,406	D	
Common Stock			06/05/2018		S		918(2)	D	\$54.94 ⁽⁹⁾	109,482	I	By Trust
Common Stock										19,500	I	By Spouse
Common Stock										60,946	I	See footnote ⁽¹⁰⁾
		Tab	le II - Derivative	Securities Ac	quired,	Dispo	sed of, or Bene	ficially Ow	ned			

	(e.g., puts, calls, warrants, options, convertible securities)																						
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	Execution Date,	(Instr. 8)	Instr. 8) S				quired (A) or	d (A) or Expiration Date Derivative Security (Instr. 3 and 4)		red (A) or Expiration Date		Derivative Security (Instr. 3 and 4)								10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title		Owned Following Reported Transaction(s) (Instr. 4)		4)									
Stock Option (Right to Buy)	\$3.6	06/04/2018		М			10,320	(11)	03/11/2019	Common Stock	10,320	\$0.00	361,181	D									
Stock Option (Right to Buy)	\$3.6	06/05/2018		М			10,320	(11)	03/11/2019	Common Stock	10,320	\$0.00	350,861	D									

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Shares sold pursuant to a 10b5-1 plan.
- 3. The shares were sold at prices ranging from \$53.80 to \$54.775. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$54.80 to \$55.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$54.05 to \$54.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$55.00 to \$55.45. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$54.45 to \$55.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$55.45 to \$55.75. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$54.60 to \$55.575. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 11. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/05/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repor	ting Person [*]						ind Ticker o		g Symbol							nip of Reporting Poplicable)	erson(s) to	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date o 06/06/20		st Transact	ction (Mon	th/Day/Ye	ar)						Officer (give title	below)	cutive Of	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	t, Date of C	Original F	iled (Mont	th/Day/	Year)			6. 1		or Joint/Group F Form filed by On				
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	ore than O	ne Repor	ting Person	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	ivative	e Securi	ities Ac	quired,	Disp	osed of	, or Bene	eficially Ow	ned						
1. Title of Security (Instr. 3)					2. Transact		2A. Deemed Execution		. Transact Code (Instr		4. Securit		ed (A) or Dispose	ed Of (D)	Bei	Amount of Securiti		Direct (D)	ship Form: or Indirect	7. Nature of Indirect
					(Month/Day		if any (Month/Day	y/Year)	ode	v	Amount		(A) or (D)	Price		lowing Reported nsaction(s) (Instr.		(I) (Instr. 4	1)	Beneficial Ownership (Instr. 4)
Common Stock					06/06/2	018			F		6,3	373(1)	D	\$56.6		2,846,033			D	
Common Stock																109,482			I	By Family Partnership
Common Stock																19,500			I	By Spouse
Common Stock																60,946			I	See footnote ⁽²⁾
				Table I					,	•	,	or Benefi e securit	icially Owne	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securi	mber of Der rities Acquir osed of (D) (5)	red (A) or	6. Date I Expirati (Month/I	on Date	•		d Amount of Sec Security (Instr.		derlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Beneficia	re F	0. Ownership orm: Direct D) or Indirect) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)))	Date Exercisa		Expiration Date	Title		Amount Number Shares			Owned Followin Reported Transact (Instr. 4)	d tion(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/08/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person*		and Ticker or Trace N INC FGEN		ol				tionship of Reporting Person(s all applicable) Director) to Issuer 10% Ow	ner	
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earlie 06/20/2018	est Transaction (M	Officer (give title below)	le below) Other (specify below) Chief Executive Officer						
409 ILLINOIS ST.			4. If Amendmer	nt, Date of Origina	l Filed (Mo	onth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Т	able I - Non-Derivativ	/e Securities	Acquire	d, Disp	oosed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3))		2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (In:		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr 4)
Common Stock			06/20/2018		М		10,320	A	\$3.6	2,856,353	D	
Common Stock			06/20/2018		S		7,701(1)	D	\$63.31(2)	2,848,652	D	
Common Stock			06/20/2018		S		11,199(1)	D	\$63.79(3)	2,837,453	D	
Common Stock			06/20/2018		S		798(1)	D	\$63.55(4)	108,684	I	By Family Partnership
Common Stock			06/20/2018		S		120(1)	D	\$63.97(5)	108,564	I	By Family Partnership
Common Stock			06/21/2018		М		10,320	A	\$3.6	2,847,773	D	
Common Stock			06/21/2018		S		15,172(1)	D	\$63.54(6)	2,832,601	D	
Common Stock			06/21/2018		S		3,728(1)	D	\$64.08 ⁽⁷⁾	2,828,873	D	
Common Stock			06/21/2018		S		918(1)	D	\$63.6(8)	107,646	I	By Family Partnership
Common Stock										19,500	I	By Spouse
								1		60,946	I	See footnote(9

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Day (Month/Day/Y	ate		. Title and Amount of Securities Underlying lerivative Security (Instr. 3 and 4)		derivative	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	06/20/2018		М			10,320	(10)	03/11/2019	Common Stock	10,320	\$0.00	340,541	D	
Stock Option (Right to Buy)	\$3.6	06/21/2018		М			10,320	(10)	03/11/2019	Common Stock	10,320	\$0.00	330,221	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$62.55 to \$63.525. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$63.55 to \$64.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$62.90 to \$63.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$63.95 to \$63.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$63.10 to \$63.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$64.00 to \$64.225. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$63.20 to \$63.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

10. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/22/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Name and Address of Render Thomas B (Last)	eporting Person* (First)	(Middle)	FIBROGE	and Ticker or Trace N INC FGEN est Transaction (M]			(Check	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director 10% Owner X Officer (give title below) Other (specify below) Chief Executive Officer				
C/O FIBROGEN, INC. 409 ILLINOIS ST.			4. If Amendme	4. If Amendment, Date of Original Filed (Month/Day/Year) 6. Individ							neck Applicable Line) rting Person One Reporting Person		
(Street) SAN FRANCISCO	CA	94158								Tomi med by More than	One reporting reason		
(City)	(State)	(Zip)											
		Table	I - Non-Derivati	ve Securities	Acquire	d, Disp	osed of, or Ben	eficially O	wned				
1. Title of Security (Instr. 3	3)		2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	d (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial	
		, , ,	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)		Ownership (Instr. 4)		
Common Stock			07/05/2018		М		10,320	A	\$3.6	2,839,193	D		
Common Stock			07/05/2018		S		13,500(1)	D	\$63.97(2)	2,825,693	D		
Common Stock			07/05/2018		S		5,400(1)	D	\$64.62(3)	2,820,293	D		
Common Stock			07/05/2018		S		818(1)	D	\$63.92(4)	106,828	I	By Family Partnership	
Common Stock			07/05/2018		S		100(1)	D	\$64.75	106,728	I	By Family Partnership	
Common Stock			07/06/2018		М		10,320	A	\$3.6	2,830,613	D		
Common Stock			07/06/2018		S		1,600(1)	D	\$64.15(5)	2,829,013	D		
Common Stock			07/06/2018		S		5,940(1)	D	\$65.24(6)	2,823,073	D		
Common Stock			07/06/2018		S		8,723(1)	D	\$66.16 ⁽⁷⁾	2,814,350	D		
Common Stock			07/06/2018		S		2,637(1)	D	\$66.96(8)	2,811,713	D		
Common Stock			07/06/2018		S		600(1)	D	\$65.61 ⁽⁹⁾	106,128	I	By Family Partnership	
Common Stock			07/06/2018		S		318(1)	D	\$66.8(10)	105,810	I	By Family Partnership	
					_	$\overline{}$	1	1		1			

			'	able i -	Non-Denv	alive 3	ecuities /	toquii eu,	Dispo.	seu oi	, or Beneficially O	wileu				
1. Title of Security (Instr. 3)					2. Transaction	Exe	Deemed ecution Date,	3. Transacti Code (Instr		I. Securit Instr. 3, 4	ies Acquired (A) or Dispo 1 and 5)	` ′	5. Amount of Securit Beneficially Owned	Dire	wnership Form: ct (D) or Indirect	7. Nature of Indirect
					(Month/Day/\	(Mc	ny onth/Day/Year)	Code	v A	Amount	(A) or (D)		Following Reported Transaction(s) (Instr. 4)		nstr. 4)	Beneficial Ownership (Inst 4)
Common Stock													19,500		I	By Spouse
Common Stock													60,946		I	See footnote ⁽¹¹⁾
				Table I							or Beneficially Owr e securities)	ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)		Securities	r of Derivative Acquired (A) of (D) (Instr. 3	or Expirati	Exercisab on Date Day/Year)		7. Title and Amount of S Derivative Security (Inst		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	f 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Inst
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		piration te	Title	Amount or Number of Shares		Owned Following Reported Transaction((Instr. 4)	s)	4)
Stock Option (Right to Buy)	\$3.6	07/05/2018		М			10,320	(12)	03/	11/2019	Common Stock	10,320	\$0.00	319,901	D	
Stock Option (Right to Buy)	\$3.6	07/06/2018		м			10 320	(12)	02/	/11/2019	Common Stock	10.320	\$0.00	309,581	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$63.35 to \$64.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$64.35 to \$65.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$63.50 to \$64.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$63.75 to \$64.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$64.75 to \$65.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$65.75 to \$66.725. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$66.80 to \$67.275. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$64.925 to \$65.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares were sold at prices ranging from \$66.70 to \$67.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 11. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 12. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/06/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep	orting Person*					and Ticker or Trac		ol				ionship of Reporting Person(all applicable) Director	s) to Issuer	nor
(Last) C/O FIBROGEN, INC.	(First)	(N	1iddle)		Date of Earli 7/18/2018	est Transaction (M	onth/Day/Y	ear)			X	Officer (give title below		pecify below)
409 ILLINOIS ST.				4.	If Amendme	nt, Date of Origina	Filed (Mo	nth/Day/	Year)		6. Indiv	idual or Joint/Group Filing (0 Form filed by One Rep		
(Street) SAN FRANCISCO	CA	92	4158									Form filed by More tha	n One Reporting Person	
(City)	(State)	(Z	ip)											
			Т	able I - Non	n-Derivativ	e Securities /	cquirec	d, Disp	osed of, or Be	neficially O	wned			
1. Title of Security (Instr. 3)				Date		2A. Deemed Execution Date,	3. Transac Code (Ins		4. Securities Acqui (Instr. 3, 4 and 5)	red (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
				(Mor	onth/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock				07	7/18/2018		M		10,320	A	\$3.6	2,822,033	D	
Common Stock				07	07/18/2018		S		8,100(1)	D	\$65.19(2)	2,813,933	D	
Common Stock				07	07/18/2018		S		10,800(1)	D	\$65.7(3)	2,803,133	D	
Common Stock				07	07/18/2018		S		918(1)	D	\$65.48(4)	104,892	I	By Family Partnership
Common Stock				07	07/19/2018		M		10,320	A	\$3.6	2,813,453	D	
Common Stock				07	07/19/2018		S		18,800(1)	D	\$64.34(5)	2,794,653	D	
Common Stock				07	07/19/2018		S		100(1)	D	\$64.8	2,794,553	D	
Common Stock				07	07/19/2018		S		918(1)	D	\$64.27(6)	103,974	I	By Family Partnership
Common Stock												19,500	I	By Spouse
Common Stock												60,946	I	See footnote ⁽⁷⁾
									sed of, or Bene nvertible secur		ned			
1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of 2. (Month/Day/Year) 3. Transaction Date (Month/Day/Year) (Month/Day/Year) 4. Transaction Execution Date, if any (Month/Day/Year)					Secu	umber of Derivative rities Acquired (A) osed of (D) (Instr. 3 d 5)	or Expira	e Exercis ition Date n/Day/Yea	Derivativ	and Amount of S ve Security (Ins	Securities Underly tr. 3 and 4)	Derivative deriv Security (Instr. Secu		11. Nature of Indirect Beneficial Ownership (Instr.

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	07/18/2018	M			10,320	(8)	03/11/2019	Common Stock	10,320	\$0.00	299,261	D	
Stock Option (Right to Buy)	\$3.6	07/19/2018	M			10,320	(8)	03/11/2019	Common Stock	10,320	\$0.00	288,941	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$64.40 to \$65.35. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$65,40 to \$66,00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$65.15 to \$65.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$63.75 to \$64.70. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price. 6. The shares were sold at prices ranging from \$63.75 to \$64.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/20/2018

** Signature of Reporting Person

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep	orting Person*					e and Ticker or Trac EN INC [FGEN		ol				tionship of Reporting Person(all applicable) Director	s) to Issuer	nor
(Last) C/O FIBROGEN, INC.	(First)	(N	Middle)		3. Date of Ea 08/01/2018	rliest Transaction (M	onth/Day/Y	'ear)			X	Officer (give title below		pecify below)
409 ILLINOIS ST.					4. If Amendm	ent, Date of Origina	I Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filing (
(Street) SAN FRANCISCO	CA	94	4158									Form filed by More tha	n One Reporting Person	
(City)	(State)	(Z	ip)											
			Т	able I - No	on-Deriva	ive Securities	Acquire	d, Disp	oosed of, or B	eneficially C	wned			
1. Title of Security (Instr. 3)				D	. Transaction	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquilinstr. 3, 4 and 5)	uired (A) or Disp	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
				("	Month/Day/Yea	r) if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock					08/01/2018		М		10,320	A	\$3.6	2,804,873	D	
Common Stock					08/01/2018		S		13,660(1)	D	\$62.95(2)	2,791,213	D	
Common Stock					08/01/2018		S		5,240(1)	D	\$63.54 ⁽³⁾	2,785,973	D	
Common Stock					08/01/2018		S		918(1)	D	\$63.08(4)	103,056	I	By Family Partnership
Common Stock					08/02/2018		M		10,320	A	\$3.6	2,796,293	D	
Common Stock					08/02/2018		S		11,600(1)	D	\$62.71 ⁽⁵⁾	2,784,693	D	
Common Stock					08/02/2018		S		7,300(1)	D	\$63.19(6)	2,777,393	D	
Common Stock					08/02/2018		S		918(1)	D	\$62.88(7)	102,138	I	By Family Partnership
Common Stock												19,500	I	By Spouse
Common Stock												60,946	I	See footnote ⁽⁸⁾
				Table II -		e Securities Ac s, calls, warran					ned			
1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of 2. (Month/Day/Year) 3. Transaction Date Execution Date, if any (Month/Day/Year)					Se Di:	Number of Derivative curities Acquired (A) sposed of (D) (Instr. 3 and 5)	or Expira	e Exercis ation Dat h/Day/Ye	te Derivat	and Amount of ive Security (Ins	Securities Underl tr. 3 and 4)	Derivative deriv Security (Instr. Secu		Indirect

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	08/01/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	278,621	D	
Stock Option (Right to Buy)	\$3.6	08/02/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	268,301	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$62.45 to \$63.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$63.45 to \$63.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$62.60 to \$63.525. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer. full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$62.05 to \$63.025. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$63.05 to \$63.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$62.25 to \$63.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/03/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person [*]				FIBROGE	e and Ticker or Trac EN INC [FGEN]					tionship of Reporting Pers all applicable) Director	son(s) to Issue	r 10% Owi	ner
(Last) C/O FIBROGEN, INC.	(First)	(M	/liddle)		3. Date of Ear 08/20/2018	liest Transaction (M	lonth/Day/\	rear)			X		elow) of Executive (٠.	pecify below)
409 ILLINOIS ST.					4. If Amendm	ent, Date of Origina	al Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filir Form filed by One I	•	*	
(Street) SAN FRANCISCO	CA	92	4158									Form filed by More	than One Rep	porting Person	
(City)	(State)	(Z	(ip)												
			Т	able I - N	Non-Derivat	ive Securities	Acquire	d, Dis	posed of, or Be	neficially C	wned				
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Yea	2A. Deemed Execution Date, r) if any	3. Transa Code (Ins		4. Securities Acqu (Instr. 3, 4 and 5)	ired (A) or Disp	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported		ership Form: (D) or Indirect	7. Nature of Indirect Beneficial
					(мониллаултеа	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 a		r. 4)	Ownership (Instr.
Common Stock					08/20/2018		М		10,320	A	\$3.6	2,787,713	D		
Common Stock					08/20/2018		S		14,897(1)	D	\$59.83 ⁽²⁾	2,772,816		D	
Common Stock					08/20/2018		S		4,003(1)	D	\$60.36(3)	2,768,813		D	
Common Stock					08/20/2018		S		918(1)	D	\$59.82(4)	101,220		I	By Family Partnership
Common Stock					08/21/2018		M		10,320	A	\$3.6	2,779,133		D	
Common Stock					08/21/2018		S		4,365(1)	D	\$60 ⁽⁵⁾	2,774,768		D	
Common Stock					08/21/2018		S		14,535(1)	D	\$60.71(6)	2,760,233		D	
Common Stock					08/21/2018		S		918(1)	D	\$60.59(7)	100,302		I	By Family Partnership
Common Stock											19,500 I By			By Spouse	
Common Stock											60,946 I			See footnote ⁽⁸⁾	
				Table II		e Securities Ac s, calls, warran					ned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of		3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code 5. Se	Number of Derivative curities Acquired (A) sposed of (D) (Instr. 3 and 5)	6. Dat		sable and 7. Title te Derivat	-	Securities Underl tr. 3 and 4)	Derivative d Security (Instr. S	. Number of erivative ecurities eneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	08/20/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	257,981	D	
Stock Option (Right to Buy)	\$3.6	08/20/2018	M			10,320	(9)	03/11/2019	Common Stock	10,320	\$0.00	247,661	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$59.25 to \$60.225. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$60.25 to \$60.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$59.25 to \$60.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$59.25 to \$60.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$60.225 to \$61.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 7. The shares were sold at prices ranging from \$60.15 to \$61.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

08/22/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Repo	ting Person [*]						nd Ticker or T <u>INC</u> [FGE		Symbol							hip of Reporting Papplicable) Director	erson(s) t	to Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 09/04/20		t Transaction	(Mont	h/Day/Yea	ır)					X	Officer (give title	,	cutive Offic	Other (spe	ecify below)
409 ILLINOIS ST.					4. If Amei	ndment,	, Date of Orig	inal Fi	led (Month	n/Day/	Year)			6.	Individua X	I or Joint/Group F Form filed by On			le Line)	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	ore than C	One Reportin	g Person	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	vative	Securitie	s Ac	quired,	Disp	osed of	, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date (Month/Day		2A. Deemed Execution Dat if any		Transaction		4. Securi (Instr. 3,		ed (A) or Dispos	ed Of (D)	Be	Amount of Securiti eneficially Owned		6. Ownership Direct (D) or (I) (Instr. 4)		7. Nature of Indirect Beneficial
					(Month/Day		(Month/Day/Ye	ar) C	ode \	,	Amount		(A) or (D)	Price		ansaction(s) (Instr.		(I) (INSTr. 4)		Ownership (Instr. 4)
Common Stock					09/04/20	018			F		2,2	286(1)	D	\$61.0)5	2,757,947		D		
Common Stock					09/06/20	018			F		6,3	373(1)	D	\$57.	3	2,751,574		D		
Common Stock																100,302		I		By Family Partnership
Common Stock																19,500		I		By Spouse
Common Stock																60,946		I		See footnote ⁽²⁾
				Table I			Securities A						icially Own ties)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securit	nber of Derivat ties Acquired (sed of (D) (Inst	(A) or	6. Date E Expiratio (Month/D	n Date	•		d Amount of Se Security (Instr.		nderlying	8. Price of Derivative Security (Instr. 5)	9. Numb derivativ Securitie Benefici	ve Forres (D)	Ownership m: Direct or Indirect nstr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisa		Expiration Date	Title		Amour Numbe Shares	r of		Owned Followin Reporte Transact (Instr. 4)	tion(s)		4)

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	eporting Person [*]		<u>FIBROGE</u>	and Ticker or Trace N INC [FGEN]					tionship of Reporting Person(s all applicable) Director) to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	09/06/2018	est Transaction (M	iontn/Day/1	rear)			X	,	Other (s	pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	al Filed (Mo	onth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C Form filed by One Repo		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Table	I - Non-Derivati	ve Securities	Acquire	d, Disp	posed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3	3)		2. Transaction Date Execution Date, (Month/Day/Year) if any							5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
			(Month/Day/Teal)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (111511: 4)	Ownership (Instr.
Common Stock			09/06/2018		М		10,320	A	\$3.6	2,761,894	D	
Common Stock			09/06/2018		S		12,480(1)	D	\$57.73(2)	2,749,414	D	
Common Stock			09/06/2018		S		2,820(1)	D	\$58.85(3)	2,746,594	D	
Common Stock			09/06/2018		S		3,600(1)	D	\$59.77(4)	2,742,994	D	
Common Stock			09/06/2018		S		718(1)	D	\$57.66 ⁽⁵⁾	99,584	I	By Family Partnership
Common Stock			09/06/2018		S		200(1)	D	\$59.08 ⁽⁶⁾	99,384	I	By Family Partnership
Common Stock			09/07/2018		М		10,320	A	\$3.6	2,753,314	D	
Common Stock			09/07/2018		S		15,495(1)	D	\$56.6(7)	2,737,819	D	
Common Stock			09/07/2018		S		3,405(1)	D	\$57.44(8)	2,734,414	D	
Common Stock			09/07/2018		s		718(1)	D	\$56.58 ⁽⁹⁾	98,666	I	By Family Partnership
Common Stock		09/07/2018		S		200(1)	D	\$57.3(10)	98,466	I	By Family Partnership	
Common Stock										19,500	I	By Spouse
			1	1			1			1	1	

			Т	able I -	Non-Deriv	ative Se	curities A	Acquired,	Dispos	sed of	, or Beneficially Ov	vned				
1. Title of Security (Instr. 3)					2. Transaction			3. Transacti Code (Instr		. Securit Instr. 3, 4	ies Acquired (A) or Dispos 1 and 5)	` ´ E	. Amount of Securit seneficially Owned	Dir	Ownership Form: rect (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day/	rear) if any (Mon	th/Day/Year)	Code	V A	Amount	(A) or (D)		ollowing Reported ransaction(s) (Instr.)		(Instr. 4)	Ownership (Insti
Common Stock													60,946		I	See footnote ⁽¹¹⁾
				Table I				•	•		or Beneficially Own e securities)	ed				
1. Title of Derivative Security (Instr. 3)	1. Title of Derivative Security 2. 3. Transaction 3A. Deemed 4. Transaction Code 5. N									le and	7. Title and Amount of Se Derivative Security (Instr		8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficially	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Ins
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		oiration te	Title	Amount or Number of Shares		Owned Following Reported Transaction (Instr. 4)	n(s)	4)
Stock Option (Right to Buy)	\$3.6	09/06/2018		M			10,320	(12)	03/1	11/2019	Common Stock	10,320	\$0.00	237,341	D	
Stock Option (Right to Buy)	\$3.6	09/07/2018		M			10,320	(12)	03/1	11/2019	Common Stock	10,320	\$0.00	227,021	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$57.30 to \$58.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 3. The shares were sold at prices ranging from \$58.30 to \$59.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$59.45 to \$60.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$57.30 to \$58.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$58.75 to \$59.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$56.15 to \$57.10. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$57.15 to \$57.65. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 9. The shares were sold at prices ranging from \$56.35 to \$56.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 10. The shares were sold at prices ranging from \$57.00 to \$57.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 11. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 12. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

Date

09/07/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	orting Person [*]			and Ticker or Trac <u>VINC</u> [FGEN		I			(Chec	ationship of Reporting Person(s) k all applicable)	to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earlie 09/19/2018	est Transaction (M	onth/Day/Y	ear)				Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendmer	nt, Date of Origina	l Filed (Mo	nth/Day/	Year)			vidual or Joint/Group Filing (Ch X Form filed by One Repor	ting Person	
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Table I -	Non-Derivativ	e Securities A	Acquired	l, Disp	osed of, or Ben	eficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transac Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	d (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			09/19/2018		М		10,320	A	\$3.6	2,744,734	D	
Common Stock			09/19/2018		S		11,408 ⁽¹⁾	D	\$56.45 ⁽²⁾	2,733,326	D	
Common Stock			09/19/2018		S		7,492(1)	D	\$57.5 ⁽³⁾	2,725,834	D	
Common Stock			09/19/2018		S		710(1)	D	\$56.71 ⁽⁴⁾	97,756	I	By Family Partnership
Common Stock			09/19/2018		S		208(1)	D	\$57.48 ⁽⁵⁾	97,548	I	By Family Partnership
Common Stock			09/20/2018		М		10,320	A	\$3.6	2,736,154	D	
Common Stock			09/20/2018		S		1,291(1)	D	\$57.36(6)	2,734,863	D	
Common Stock			09/20/2018		S		17,609(1)	D	\$58.84 ⁽⁷⁾	2,717,254	D	
Common Stock			09/20/2018		S		9(1)	D	\$57.64 ⁽⁸⁾	97,539	I	By Family Partnership
Common Stock			09/20/2018		S		909(1)	D	\$58.88 ⁽⁹⁾	96,630	I	By Family Partnership
Common Stock										19,500	I	By Spouse
Common Stock										60,946	I	See footnote ⁽¹⁰⁾

	Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned Title of Security (Instr. 3) 2. Transaction 2A. Deemed 3. Transaction 4. Securities Acquired (A) or Disposed Of (D) 5. Amount of Securities 6. Ownership Form: 7. Nature of																
1. Title of Security (Instr. 3)					Date E		Execution Date,			4. Securit (Instr. 3, 4	ties Acquired (A) 4 and 5)	or Dispose		5. Amount of Securiti Beneficially Owned	Dii	Ownership Form: ect (D) or Indirect	7. Nature of Indirect
					(Month/Day/	(Mor	y th/Day/Year)	Code	v	Amount	(A)	or (D)	Price	Following Reported Transaction(s) (Instr. 4)		(Instr. 4)	Beneficial Ownership (Instr. 4)
			Table I							or Beneficial e securities)	•	ed					
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Derivative Securities Acquired (A) of Disposed of (D) (Instr. 3, 4 and 5)		r Expirat	Exercisa ion Date Day/Yea		7. Title and Amo Derivative Secu			8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficially	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr.	
	Derivative Security			Code	v	(A)	(D)	Date Exercis		xpiration late	Title		Amount or Number of Shares		Owned Following Reported Transaction (Instr. 4)	(s)	4)
Stock Option (Right to Buy)	\$3.6	09/19/2018		М	10,320		(11)	0	3/11/2019	Common S	Stock	10,320	\$0.00	216,701	D		
Stock Option (Right to Buy)	\$3.6	09/20/2018		M	10,320			(11)	0	3/11/2019	Common S	Stock	10,320	\$0.00	206,381	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$56.10 to \$56.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$57.05 to \$57.825. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$56.20 to \$56.975. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$57.10 to \$57.875. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$56.85 to \$57.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$58.20 to \$59.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$57.45 to \$57.80. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$58.70 to \$59.00. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 11. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

09/21/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	orting Person [*]			and Ticker or Trac <u>VINC</u> [FGEN		il			(Che	lationship of Reporting Person(s) ck all applicable) X Director	to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earlie 10/02/2018	est Transaction (M	onth/Day/Y	ear)				X Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendmer	nt, Date of Origina	l Filed (Mo	nth/Day/	Year)			dividual or Joint/Group Filing (Ch $old X$ Form filed by One Repor	ting Person	
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Table I -	Non-Derivativ	e Securities /	Acquired	l, Disp	osed of, or Ben	eficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transac Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	d (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			10/02/2018		М		10,320	A	\$3.6	2,727,574	D	
Common Stock			10/02/2018		S		8,998(1)	D	\$58.47(2)	2,718,576	D	
Common Stock			10/02/2018		S		9,902(1)	D	\$59.16 ⁽³⁾	2,708,674	D	
Common Stock			10/02/2018		S		718(1)	D	\$58.79 ⁽⁴⁾	95,912	I	By Family Partnership
Common Stock			10/02/2018		S		200(1)	D	\$59.37 ⁽⁵⁾	95,712	I	By Family Partnership
Common Stock			10/03/2018		M		10,319	A	\$3.6	2,718,993	D	
Common Stock			10/03/2018		S		8,193(1)	D	\$58.82(6)	2,710,800	D	
Common Stock			10/03/2018		S		10,707(1)	D	\$59.94(7)	2,700,093	D	
Common Stock			10/03/2018		S		307(1)	D	\$58.68(8)	95,405	I	By Family Partnership
Common Stock			10/03/2018		S		611(1)	D	\$59.89 ⁽⁹⁾	94,794	I	By Family Partnership
Common Stock										19,500	I	By Spouse
Common Stock										60,946	I	See footnote ⁽¹⁰⁾

	Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned Title of Security (Instr. 3) 2. Transaction 2. Deemed 3. Transaction 4. Securities Acquired (A) or Disposed Of (D) 5. Amount of Securities 6. Ownership Form: 7. Nature of																
1. Title of Security (Instr. 3)					Date Ex		Execution Date, C			4. Securit (Instr. 3, 4	ies Acquired (4 and 5)	(A) or Dispose	ed Of (D)	5. Amount of Securiti Beneficially Owned	Di	Ownership Form: rect (D) or Indirect	7. Nature of Indirect
					(Month/Day/	(Mor	y th/Day/Year)	Code	v	Amount	(4	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 4)		(Instr. 4)	Beneficial Ownership (Instr. 4)
			Table I					•		or Benefici e securitie	•	ed					
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	5. Number of Derivative Securities Acquired (A) o Disposed of (D) (Instr. 3, 4 and 5)		r Expirati	Exercisa ion Date Day/Year		7. Title and A Derivative Se		curities Underly 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficiall	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr.	
	Derivative Security			Code	v	(A)	(D)	Date Exercis		xpiration ate	Title		Amount or Number of Shares		Owned Following Reported Transaction (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	10/02/2018		М	10,320		(11)	03	3/11/2019	Commo	on Stock	10,320	\$0.00	196,061	I D		
Stock Option (Right to Buy)	\$3.6	10/03/2018		M	10,319			(11)	03	3/11/2019	Commo	on Stock	10,319	\$0.00	185,742	2 D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$57.955 to \$58.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$58.96 to \$59.61. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$58.22 to \$59.15. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$59.23 to \$59.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$58.33 to \$59.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$59.33 to \$60.29. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$58.62 to \$58.73. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$59.73 to \$60.19. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 11. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

10/04/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person [*]			and Ticker or Trac <u>VINC</u> [FGEN		ol				ationship of Reporting Person(s call applicable) Oirector) to Issuer 10% Ow	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earlie 10/18/2018	est Transaction (M	onth/Day/Y	ear)			X	Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendmer	nt, Date of Origina	l Filed (Mo	nth/Day/	/Year)		6. Indiv	vidual or Joint/Group Filing (C		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	•	
(City)	(State)	(Zip)	-									
		Table I -	Non-Derivativ	e Securities /	Acquire	d, Disp	osed of, or Ben	eficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transac Code (Ins	ction tr. 8)	4. Securities Acquire (Instr. 3, 4 and 5)	d (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			10/18/2018		М		10,319	A	\$3.6	2,710,412	D	
Common Stock			10/18/2018		S ⁽¹⁾		13,136	D	\$54.23 ⁽²⁾	2,697,276	D	
Common Stock			10/18/2018		S ⁽¹⁾		5,364	D	\$55.13 ⁽³⁾	2,691,912	D	
Common Stock			10/18/2018		S ⁽¹⁾		400	D	\$55.9	2,691,512	D	
Common Stock			10/18/2018		S ⁽¹⁾		718	D	\$54.36(4)	94,076	I	By Family Partnership
Common Stock			10/18/2018		S ⁽¹⁾		200	D	\$55.29 ⁽⁵⁾	93,876	I	By Family Partnership
Common Stock			10/19/2018		M		10,319	A	\$3.6	2,701,831	D	
Common Stock			10/19/2018		S ⁽¹⁾		6,100	D	\$52.96(6)	2,695,731	D	
Common Stock			10/19/2018		S ⁽¹⁾		6,300	D	\$53.74(7)	2,689,431	D	
Common Stock			10/19/2018		S ⁽¹⁾		4,700	D	\$54.78(8)	2,684,731	D	
Common Stock			10/19/2018		S ⁽¹⁾		1,800	D	\$55.57(9)	2,682,931	D	
Common Stock			10/19/2018		S ⁽¹⁾		618	D	\$53.2(10)	93,258	I	By Family Partnership

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned												
1. Title of Security (Instr. 3)	Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect		
			Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)		
Common Stock	10/19/2018		S ⁽¹⁾		300	D	\$54.69(11)	92,958	I	By Family Partnership		
Common Stock								19,500	I	By Spouse		
Common Stock								60,946	I	See footnote ⁽¹²⁾		

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	Conversion Date Execution Date (Month/Day/Year) if any (Month/Day/Year) (Month/Day/Year)		Execution Date,	(Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)				7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		Derivative	derivative Securities Beneficially	(D) or Indirect	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	10/18/2018		M			10,319	(13)	03/11/2019	Common Stock	10,319	\$0.00	175,423	D	
Stock Option (Right to Buy)	\$3.6	10/19/2018		М			10,319	(13)	03/11/2019	Common Stock	10,319	\$0.00	165,104	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$53.73 to \$54.71. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$54.765 to \$55.50. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$53.90 to \$54.77. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$55.26 to \$55.31. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$52.305 to \$53.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$53.31 to \$54.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$54.31 to \$55.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$55.31 to \$55.77. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares were sold at prices ranging from \$52.90 to \$53.75. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 11. The shares were sold at prices ranging from \$54.15 to \$55.01. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 12. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 13. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

10/19/2018

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Name and Address of Reporting Person* Neff Thomas B					FIBROG	ie and Ticker or Trad EN INC [FGEN]			(Check	Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director 10% Owner						
(Last) C/O FIBROGEN, INC.	(First)	(N	/liddle)		3. Date of Earliest Transaction (Month/Day/Year) 11/01/2018							Officer (give title below) Other (spec		pecify below)			
409 ILLINOIS ST.					4. If Amendn	ent, Date of Origina	al Filed (Mo	onth/Day	/Year)		Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person						
(Street) SAN FRANCISCO	CA	92	4158														
(City)	(State)	(Z	(ip)														
			Т	able I - I	Non-Deriva	tive Securities	Acquire	d, Dis _l	posed of, or	Beneficially C	Owned						
1. Title of Security (Instr. 3)				- 1	2. Transaction Date (Month/Day/Yea	2A. Deemed Execution Date, r) if any	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Di (Instr. 3, 4 and 5)		osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	Direct	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial		
					(Month/Day/Tear)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3		tr. 4)	Ownership (Instr		
Common Stock					11/01/2018		М		10,319	A	\$3.6	2,693,250		D			
Common Stock					11/01/2018		S ⁽¹⁾		14,400	D	\$43.92(2)	2,678,850		D			
Common Stock					11/01/2018		S ⁽¹⁾		4,500	D	\$44.42(3)	2,674,350		D			
Common Stock					11/01/2018		S ⁽¹⁾		918	D	\$44.08(4)	92,040		I	By Family Partnership		
Common Stock					11/02/2018		M		10,319	A	\$3.6	2,684,669		D			
Common Stock					11/02/2018		S ⁽¹⁾		17,800	D	\$44.56(5)	2,666,869		D			
Common Stock					11/02/2018		S ⁽¹⁾		1,100	D	\$45.18(6)	2,665,769		D			
Common Stock					11/02/2018		S ⁽¹⁾		918	D	\$44.61 ⁽⁷⁾	91,122		I	By Family Partnership		
Common Stock												19,500		I	By Spouse		
Common Stock												60,946		I	See footnote ⁽⁸⁾		
				Table II		e Securities Ac s, calls, warran					ned						
1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise (Month/Day/Year) 2. Conversion or Exercise (Month/Day/Year) (Instr. 8) 4. Transaction Execution Date, if any (Month/Day/Year)					ction Code 5.	Number of Derivative curities Acquired (A) sposed of (D) (Instr. and 5)	e 6. Dat		sable and 7. Ti	tle and Amount of vative Security (Ins		Derivative Security (Instr. S). Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect		

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	11/01/2018	M			10,319	(9)	03/11/2019	Common Stock	10,319	\$0.00	154,785	D	
Stock Option (Right to Buy)	\$3.6	11/02/2018	M			10,319	(9)	03/11/2019	Common Stock	10,319	\$0.00	144,466	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$43.25 to \$44.24. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$44.27 to \$44.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$43.77 to \$44.46. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$44.03 to \$45.015. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$45.03 to \$45.52. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$44.11 to \$44.91. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

11/02/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person [*]			and Ticker or Trac		ol				tionship of Reporting Person(s all applicable) Director) to Issuer	iner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 11/20/2018	est Transaction (M	lonth/Day/Y	'ear)			X	Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	vidual or Joint/Group Filing (C		
(Street)			_							Form filed by More than	•	
SAN FRANCISCO	CA	94158	_									
(City)	(State)	(Zip)										
		Table	- Non-Derivati	ve Securities	Acquire	d, Dis	oosed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			11/20/2018		М		10,319	A	\$3.6	2,676,088	D	
Common Stock			11/20/2018		S ⁽¹⁾		2,700	D	\$38.29(2)	2,673,388	D	
Common Stock			11/20/2018		S ⁽¹⁾		15,800	D	\$39.41(3)	2,657,588	D	
Common Stock			11/20/2018		S ⁽¹⁾		400	D	\$39.95(4)	2,657,188	D	
Common Stock			11/20/2018		S ⁽¹⁾		818	D	\$39.2(5)	90,304	I	By Family Partnership
Common Stock			11/20/2018		S ⁽¹⁾		100	D	\$39.65	90,204	I	By Family Partnership
Common Stock			11/21/2018		М		10,319	A	\$3.6	2,667,507	D	
Common Stock			11/21/2018		S ⁽¹⁾		18,900	D	\$39.47(6)	2,648,607	D	
Common Stock			11/21/2018		S ⁽¹⁾		918	D	\$39.47(7)	89,286	I	By Family Partnership
Common Stock										19,500	I	By Spouse
Common Stock										60,946	I	See footnote ⁽⁸⁾
Common Stock		Tabl					sed of, or Bene onvertible secur		ned	00,740	1	See Tootho

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)			Derivative quired (A) or (D) (Instr. 3,	6. Date Exerc Expiration Da (Month/Day/Y	ite	7. Title and Amount of Sec Derivative Security (Instr. 3			9. Number of derivative Securities Beneficially Owned	(D) or Indirect	Indirect
	Security			Code	v	(A)	(A) (D)		Expiration Date	Title	Amount or Number of Shares		Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	11/20/2018		М			10,319	(9)	03/11/2019	Common Stock	10,319	\$0.00	134,147	D	
Stock Option (Right to Buy)	\$3.6	11/21/2018		M			10,319	(9)	03/11/2019	Common Stock	10,319	\$0.00	123,828	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$37.85 to \$38.84. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$38.90 to \$39.88. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$39.895 to \$39.97. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$38.50 to \$39.44. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$39.00 to \$39.99. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$39.10 to \$39.93. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

11/21/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Repo	orting Person*						Ticker or Tra	•	Symbol						ck all ap	ip of Reporting Peoplicable)	erson(s) to	slssuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 12/03/20		ransaction (M	¶onth/[Day/Yea	ır)						Officer (give title	below) nief Exec	utive C	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment, D	ate of Origina	al Filed	d (Month	n/Day/	Year)			6. Inc		or Joint/Group Fi			*	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo		-		
(City)	(State)	(Zi	p)																	
			Т	able I - I	Non-Deri	vative S	Securities	Acqı	uired,	Disp	osed of	, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)					2. Transact Date	Exe	Deemed ecution Date,		ransactio e (Instr.		4. Securit		d (A) or Dispos	sed Of (D)	Ben	mount of Securiti	`` ı	Direct (rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day		iny onth/Day/Year)	Cod	e V	,	Amount		(A) or (D)	Price		lowing Reported nsaction(s) (Instr.		(I) (Instr	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					12/03/20	018		1	F		2,2	287(1)	D	\$43.93		2,646,320			D	
Common Stock					12/06/20	018]	F		6,3	73(1)	D	\$40.93		2,639,947			D	
Common Stock					12/06/20	018		N	М		11	,002	A	\$3.6		2,650,949			D	
Common Stock					12/06/20	018		S	(2)		18	,937	D	\$40.75(3)		2,632,012			D	
Common Stock					12/06/20	018		S	(2)		9,	227	D	\$41.29 ⁽⁴⁾		2,622,785			D	
Common Stock					12/06/20	018		S	(2)		1,	836	D	\$40.91(5)		87,450			I	By Family Partnership
Common Stock																19,500			I	By Spouse
Common Stock																60,946			I	See footnote ⁽⁶⁾
				Table I			curities Ad						icially Own	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securities	er of Derivative s Acquired (A) I of (D) (Instr.	or E	6. Date Expiratio	n Date			d Amount of Se Security (Instr		erlying	8. Price of Derivative Security (Instr. 5)	9. Numbe derivative Securitie Beneficia	e	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)		Date Exercisat		Expiration Date	Title		Amount o Number o Shares			Owned Followin Reported Transacti (Instr. 4)	ion(s)		4)
		1																		

	Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)														
Title of Derivative Security nstr. 3) 2. Conversion or Exercise Price of Derivative Security (Month/Day/Year) 2. Conversion or Exercise Price of Derivative Security (Month/Day/Year) 2. Conversion or Exercise Price of Date (Month/Day/Year) 3. Transaction Code (Instr. 8) 4. Transaction Code (Instr. 8) 5. Number of Derivative Security (Instr. 3 and 4) Expiration Date (Month/Day/Year) 6. Date Exercisable and Expiration Date (Month/Day/Year) 6. Derivative Security (Instr. 3 and 4) Expiration Date (Month/Day/Year) 6. Derivative Security (Instr. 3 and 4) Expiration Date (Month/Day/Year) 9. Number of derivative Security (Instr. 5) 10. Ownership Form: Direct (D) or Indirect Beneficially Ownership (Instr. 4) Ownership (Instr. 4) Ownership (Instr. 4) Ownership (Instr. 4)															
	Derivative Security Owned Following Reported Number of Transaction(s) Code V (A) (D) Exercisable Date Title Shares (Instr. 4)												4)		
Stock Option (Right to Buy)															

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. Shares sold pursuant to a 10b5-1 plan.
- 3. The shares were sold at prices ranging from \$40.06 to \$41.05. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$41.07 to \$41.92. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$40.50 to \$41.38. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 7. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

12/06/2018

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person [*]		I .	and Ticker or Trac N INC [FGEN	0 ,	ol				tionship of Reporting Person(s all applicable) Director) to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 01/03/2019	est Transaction (M	onth/Day/Y	ear)			X	Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C	,	
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Table	I - Non-Derivati	ve Securities	Acquired	l, Disp	oosed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date	2A. Deemed Execution Date,	3. Transac Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			01/03/2019		М		30,000	A	\$3.6	2,652,785	D	
Common Stock			01/03/2019		S ⁽¹⁾		11,900	D	\$43.08(2)	2,640,885	D	
Common Stock			01/03/2019		S ⁽¹⁾		11,493	D	\$44.12(3)	2,629,392	D	
Common Stock			01/03/2019		S ⁽¹⁾		6,507	D	\$44.84(4)	2,622,885	D	
Common Stock			01/03/2019		S ⁽¹⁾		100	D	\$45.75	2,622,785	D	
Common Stock			01/04/2019		М		20,912	A	\$3.6	2,643,697	D	
Common Stoc			01/04/2019		S ⁽¹⁾		4,400	D	\$44.12(5)	2,639,297	D	
Common Stock			01/04/2019		S ⁽¹⁾		25,600	D	\$45.05(6)	2,613,697	D	
Common Stock										87,450	I	By Family Partnership
Common Stock										19,500	I	By Spouse
Common Stock										60,946	I	See footnote ⁽⁷⁾
		Tal	ole II - Derivative (e.g., puts				sed of, or Bene invertible secur		ned			
1. Title of Derivative Security (Instr. 3)	Conversion		ransaction Code 5. N	umber of Derivative urities Acquired (A) posed of (D) (Instr. 3	6. Date	Exercis	sable and 7. Title at	•	Securities Underl tr. 3 and 4)	ying 8. Price of 9. Nur Derivative deriva Security (Instr. Secur	tive Form: Direct	11. Nature of Indirect Beneficial

1	Price of Derivative		(Month/Day/Year)			4 and 5)						5)		(I) (Instr. 4)	Ownership (Instr.
	Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	01/03/2019		M			30,000	(8)	03/11/2019	Common Stock	30,000	\$0.00	82,826	D	
Stock Option (Right to Buy)	\$3.6	01/04/2019		M			20,912	(8)	03/11/2019	Common Stock	20,912	\$0.00	61,914	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$42.50 to \$43.475. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$43.50 to \$44.49. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$44.50 to \$45.44\$. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$43.60 to \$44.575. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$44.61 to \$45.445. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

01/07/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	porting Person [*]			and Ticker or Trac <u>VINC</u> [FGEN		ol				tionship of Reporting Person(s all applicable) Director) to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earlie 01/22/2019	est Transaction (M	lonth/Day/\	ear)			X	Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendmer	nt, Date of Origina	al Filed (Mo	nth/Day	/Year)		6. Indiv	idual or Joint/Group Filing (C		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Та	ıble I - Non-Derivativ	e Securities	Acquire	d, Dis _l	oosed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect Beneficial
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Ownership (Inst
Common Stock			01/22/2019		М		10,319	A	\$3.6	2,624,016	D	
Common Stock			01/22/2019		S ⁽¹⁾		26,450	D	\$51.93(2)	2,597,566	D	
Common Stock			01/22/2019		S ⁽¹⁾		3,550	D	\$52.42(3)	2,594,016	D	
Common Stock			01/23/2019		М		10,319	A	\$3.6	2,604,335	D	
Common Stoc			01/23/2019		S ⁽¹⁾		12,848	D	\$51.46(4)	2,591,487	D	
Common Stock			01/23/2019		S ⁽¹⁾		12,975	D	\$52.37(5)	2,578,512	D	
Common Stock			01/23/2019		S ⁽¹⁾		2,085	D	\$52.93(6)	2,576,427	D	
Common Stock			01/23/2019		S ⁽¹⁾		702	D	\$51.83(7)	86,748	I	By Family Partnership
Common Stock			01/23/2019		S ⁽¹⁾		1,390	D	\$52.59 ⁽⁸⁾	85,358	I	Family Partnership
Common Stock										19,500	I	By Spouse
Common Stock										60,946	I	See footnote(5
			Table II - Derivative (e.g., puts,				sed of, or Bene onvertible secur		ned			
Title of Derivative Security (Instr. 3)	2. Conversion D		4. Transaction Code 5. Nu (Instr. 8) Secu	ımber of Derivative rities Acquired (A)				nd Amount of S	Securities Underl rr. 3 and 4)	ying 8. Price of 9. Nur Derivative deriva		11. Nature of Indirect

	Price of	(Month/Day/Year)	if any (Month/Day/Year)		C 4		(D) (Instr. 3,	(Month/Day/Y	ear)			Security (Instr. 5)	Beneficially	(D) or Indirect (I) (Instr. 4)	Beneficial Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	01/22/2019		M			10,319	(10)	03/11/2019	Common Stock	10,319	\$0.00	51,595	D	
Stock Option (Right to Buy)	\$3.6	01/23/2019		M			10,319	(10)	03/11/2019	Common Stock	10,319	\$0.00	41,276	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$51.335 to \$52.325. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$52.33 to \$52.58. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$50.86 to \$51.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$51.86 to \$52.855. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$52.86 to \$53.105. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$50.91 to \$51.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$51.98 to \$52.92. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP. 10. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

01/24/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person*		FIBROGE 3. Date of Earli	and Ticker or Trace N INC FGEN est Transaction (M]			5. Rela (Check X		10% Owner			
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	02/07/2019						A	,	ecutive Officer		
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	ıl Filed (Mo	nth/Day	/Year)		6. Indiv	ridual or Joint/Group Filing (C Form filed by One Repo			
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person		
(City)	(State)	(Zip)											
		Table	I - Non-Derivati	ve Securities	Acquire	d, Disp	posed of, or Ben	eficially O	wned				
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial	
			(Month/Day/Tear)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (Instr. 4)	Ownership (Instr. 4)	
Common Stock			02/07/2019		М		10,319	A	\$3.6	2,680,346	D		
Common Stock			02/07/2019		S ⁽¹⁾		19,015	D	\$55.94 ⁽²⁾	2,661,331	D		
Common Stock			02/07/2019		S ⁽¹⁾		5,013	D	\$57.06(3)	2,656,318	D		
Common Stock			02/07/2019		S ⁽¹⁾		3,847	D	\$55.98(4)	81,511	D		
Common Stock			02/07/2019		S ⁽¹⁾		487	D	\$57.01(5)	81,024	D		
Common Stock			02/08/2019		M		10,319	A	\$3.6	2,666,637	D		
Common Stock			02/08/2019		S ⁽¹⁾		5,257	D	\$56.54(6)	2,661,380	D		
Common Stock			02/08/2019		S ⁽¹⁾		13,593	D	\$57.05(7)	2,647,787	D		
Common Stock			02/08/2019		S ⁽¹⁾		50	D	\$57.68	2,647,737	D		
Common Stock			02/08/2019		S ⁽¹⁾		818	D	\$56.79(8)	80,206	I	By Family Partnership	
Common Stock			02/08/2019		S ⁽¹⁾		100	D	\$57.68	80,106	I	By Family Partnership	
Common Stock										19,500	I	By Spouse	
Common Stock										60,946	I	See footnote ⁽⁹⁾	

	Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)														
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transac (Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Day (Month/Day/Y	ate	Derivative Security (Instr. 3 and 4)			9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$3.6	02/07/2019		М			10,319	(10)	03/11/2019	Common Stock	10,319	\$0.00	30,957	D	
Stock Option (Right to Buy)	\$3.6	02/08/2019		M			10,319	(10)	03/11/2019	Common Stock	10,319	\$0.00	20,638	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$55.48 to \$56.44. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$56.80 to \$57.43. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$55.54 to \$56.32. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$56.94 to \$57.17. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$55.67 to \$56.66. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$56.67 to \$57.66. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$56.58 to \$57.08. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

10. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

02/08/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re $\underline{NeffThomas\ B}$	porting Person [*]			and Ticker or Trace VINC FGEN		ol				tionship of Reporting Person(s all applicable) Director) to Issuer	vner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earlie 02/19/2019	est Transaction (M	onth/Day/Y	'ear)			X	Officer (give title below)	Other (s	pecify below)
409 ILLINOIS ST.			4. If Amendmer	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	idual or Joint/Group Filing (C Form filed by One Repo		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than		
(City)	(State)	(Zip)										
		Ta	able I - Non-Derivativ	e Securities	Acquire	d, Disp	posed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3))		2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr 4)
Common Stock			02/19/2019		М		10,319	A	\$3.6	2,658,056	D	
Common Stock			02/19/2019		S ⁽¹⁾		18,100	D	\$57.69(2)	2,639,956	D	
Common Stock			02/19/2019		S ⁽¹⁾		800	D	\$58.26(3)	2,639,156	D	
Common Stock			02/19/2019		S ⁽¹⁾		918	D	\$57.67(4)	79,188	I	By Family Partnership
Common Stock			02/20/2019		M		10,319	A	\$3.6	2,649,475	D	
Common Stock			02/20/2019		S ⁽¹⁾		9,050	D	\$56.71(5)	2,640,425	D	
Common Stock			02/20/2019		S ⁽¹⁾		9,850	D	\$57.47 ⁽⁶⁾	2,630,575	D	
Common Stock			02/20/2019		S ⁽¹⁾		500	D	\$56.76 ⁽⁷⁾	78,688	I	By Family Partnership
Common Stock			02/20/2019		S ⁽¹⁾		418	D	\$57.41(8)	78,270	I	By Family Partnership
Common Stock										19,500	I	By Spouse
										60,946	ī	See footnote(9

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Day (Month/Day/Y	ate	7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)			Beneficially	(D) or Indirect	Indirect
	Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$3.6	02/19/2019		М			10,319	(10)	03/11/2019	Common Stock	10,319	\$0.00	10,319	D	
Stock Option (Right to Buy)	\$3.6	02/20/2019		M			10,319	(10)	03/11/2019	Common Stock	10,319	\$0.00	0	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$57.34 to \$57.98. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$58.07 to \$58.47. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$57.34 to \$57.88. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$56.22 to \$57.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$57.22 to \$57.74. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$56.29 to \$57.21. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$57.35 to \$57.51. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP. 10. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

02/21/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

Name and Address of Reporting Person* Neff Thomas B						2. Issuer Name and Ticker or Trading Symbol FIBROGEN INC [FGEN]									5. Relationship of Repo (Check all applicable) X Director		erson(s) to	o Issuer	10% Own	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 03/04/20		st Transaction	(Mont	h/Day/Ye	ar)					X	Officer (give title	,	cutive Offic	٠.	ecify below)
409 ILLINOIS ST.					4. If Ame	ndment	, Date of Orig	inal Fi	led (Mon	th/Day/	Year)			6	3. Individu X	ual or Joint/Group F Form filed by On	- 1		le Line)	
(Street) SAN FRANCISCO	CA	94	158													Form filed by Mo	ore than O	one Reportin	ig Person	
(City)	(State)	(Zi	p)																	
			Т	able I -	Non-Deri	vative	e Securitie	s Ac	quired	, Disp	osed of	, or Ben	eficially Ov	vned						
1. Title of Security (Instr. 3)	Title of Security (Instr. 3)				2. Transact Date		2A. Deemed Execution Dat		Transact			curities Acquired (A) or Disposed Of (. 3, 4 and 5)			´ [1	5. Amount of Securities Beneficially Owned		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect
					(Month/Day		if any (Month/Day/Ye	ar) c	ode	v	Amount		(A) or (D)	Price	- 1	Following Reported Transaction(s) (Instr. 3 and 4)		(I) (INSTr. 4)		Beneficial Ownership (Instr. 4)
Common Stock					03/04/20	019			F		2,2	288(1)	D	\$58	3.69	2,627,787		D)	
Common Stock					03/06/2	019			F		15,0	049(1)	D	\$55	5.58	2,612,738		D)	
Common Stock																78,270		I		By Family Partnership
Common Stock																20,000		I		By Spouse
Common Stock																60,946		I		See footnote ⁽²⁾
				Table I			Securities A						icially Own ties)	ed						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ction Code	Securi	nber of Derivat ities Acquired (sed of (D) (Inst 5)	A) or	6. Date Expirati (Month/	ion Date			d Amount of Se Security (Instr.	curities Underlyi 3 and 4)		Derivative Security (Instr. 5)		re For	Ownership m: Direct or Indirect Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
	Security			Code	v	(A)	(D)		Date Exercis		Expiration Date	Title		Amount or Number of Shares			Owned Followin Reported Transact (Instr. 4)	d tion(s)		*')

Explanation of Responses:

- 1. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 2. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

Remarks:

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re	eporting Person [*]			and Ticker or Trac		ol			tionship of Reporting Person(s) all applicable) Director	to Issuer	ner	
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 03/06/2019	est Transaction (M	onth/Day/Y	'ear)			X	Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filing (Cl Form filed by One Repo		
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	•	
(City)	(State)	(Zip)	_									
		Table	I - Non-Derivati	ve Securities /	Acquire	d, Disp	oosed of, or Ben	eficially O	wned			
1. Title of Security (Instr. 3)		2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
			(Month/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock			03/06/2019		М		6,834	A	\$2.9	2,619,572	D	
Common Stock			03/06/2019		S ⁽¹⁾		9,464	D	\$55.84 ⁽²⁾	2,610,108	D	
Common Stock			03/06/2019		S ⁽¹⁾		7,836	D	\$56.84 ⁽³⁾	2,602,272	D	
Common Stock			03/06/2019		S ⁽¹⁾		1,100	D	\$57.68(4)	2,601,172	D	
Common Stock			03/06/2019		S ⁽¹⁾		818	D	\$55.81 ⁽⁵⁾	77,452	I	By Family Partnership
Common Stock			03/06/2019		S ⁽¹⁾		600	D	\$56.86 ⁽⁶⁾	76,852	I	By Family Partnership
Common Stock			03/07/2019		М		6,834	A	\$2.9	2,608,006	D	
Common Stock			03/07/2019		S ⁽¹⁾		17,200	D	\$54.9 ⁽⁷⁾	2,590,806	D	
Common Stock			03/07/2019		S ⁽¹⁾		1,200	D	\$55.47(8)	2,589,606	D	
Common Stock			03/07/2019		S ⁽¹⁾		1,318	D	\$54.89(9)	75,534	I	By Family Partnership
Common Stock			03/07/2019		S ⁽¹⁾		100	D	\$55.45	75,434	I	By Family Partnership
Common Stock										20,000	I	By Spouse

			Т	able I -	Non-Deriv	ative Se	curities A	Acquired,	Dispose	ed of,	or Beneficially Ov	/ned				
1. Title of Security (Instr. 3)					Date	Date Execution Date, C		3. Transacti Code (Instr.		(Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned		Ownership Form: rect (D) or Indirect	7. Nature of Indirect
					(Month/Day/\	ear) if any (Mont	h/Day/Year)	Code	V Am	nount	(A) or (D)		ollowing Reported ransaction(s) (Instr.)		(Instr. 4)	Ownership (Inst
Common Stock													60,946		I	See footnote ⁽¹⁰⁾
				Table I				•	•		Beneficially Own securities)	ed				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	- 1	Securities A	of Derivative acquired (A) of f (D) (Instr. 3	or Expiration			7. Title and Amount of Se Derivative Security (Instr.		8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficiall	Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Ins
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		ration 1	Title	Amount or Number of Shares		Owned Following Reported Transaction (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.9	03/06/2019		M			6,834	(11)	06/09	9/2020	Common Stock	6,834	\$0.00	334,884	4 D	
Stock Option (Right to Buy)	\$2.9	03/07/2019		M			6,834	(11)	06/09	9/2020	Common Stock	6,834	\$0.00	328,050) D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$55.50 to \$56.47. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$56.50 to \$57.49. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$57.50 to \$57.88. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$55.50 to \$56.22. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$56.70 to \$57.11. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$54.31 to \$55.29. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$55.32 to \$55.64. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$54.42 to \$55.22. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 11. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

03/08/2019

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person [*]			and Ticker or Trac		ol				tionship of Reporting Person(s all applicable) Director) to Issuer 10% Ow	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 03/20/2019	est Transaction (M	lonth/Day/Y	ear)			X	,	Other (specutive Officer	pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	al Filed (Mo	nth/Day	Individual or Joint/Group Filing (Check Applicable Line) $ X \qquad \text{Form filed by One Reporting Person} $					
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Tab	le I - Non-Derivati	ve Securities	Acquire	d, Disp	osed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
		(Month/Day/Tear)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(i) (instr. 4)	Ownership (Instr.	
Common Stock			03/20/2019		М		6,834	A	\$2.9	2,596,440	D	
Common Stock			03/20/2019		S ⁽¹⁾		11,134	D	\$55.14 ⁽²⁾	2,585,306	D	
Common Stock			03/20/2019		S ⁽¹⁾		7,266	D	\$55.83(3)	2,578,040	D	
Common Stock			03/20/2019		S ⁽¹⁾		428	D	\$55.09(4)	75,006	I	By Family Partnership
Common Stock			03/20/2019		S ⁽¹⁾		990	D	\$55.83 ⁽⁵⁾	74,016	I	By Family Partnership
Common Stock			03/21/2019		М		6,834	A	\$2.9	2,584,874	D	
Common Stock			03/21/2019		S ⁽¹⁾		9,642	D	\$55.37 ⁽⁶⁾	2,575,232	D	
Common Stock			03/21/2019		S ⁽¹⁾		8,758	D	\$55.85(7)	2,566,474	D	
Common Stock			03/21/2019		S ⁽¹⁾		1,418	D	\$55.83(8)	72,598	I	By Family Partnership
Common Stock										20,000	I	By Spouse
Common Stock										60,946	I	See footnote ⁽⁹⁾
		T	able II - Derivative (e.g., puts				sed of, or Benef nvertible securi		ned	1		1

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	(Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration Day (Month/Day/Y	ate		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		derivative	(D) or Indirect	Indirect
	Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Title Shares		Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.9	03/20/2019		М			6,834	(10)	06/09/2020	Common Stock	6,834	\$0.00	321,216	D	
Stock Option (Right to Buy)	\$2.9	03/21/2019		M			6,834	(10)	06/09/2020	Common Stock	6,834	\$0.00	314,382	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$54.48 to \$55.47. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$55.495 to \$56.23. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$54.89 to \$55.32. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$55.59 to \$56.01. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$54.65 to \$55.64. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$55.65 to \$56.18. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$55.32 to \$55.98. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

10. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

03/22/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep	porting Person [*]			and Ticker or Trac <u>VINC</u> [FGEN		ol		(Check	tionship of Reporting Person(s all applicable) Director) to Issuer				
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 04/03/2019	est Transaction (M	onth/Day/Y	ear)			X X	Officer (give title below)		ner pecify below)		
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)	I	6. Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person					
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person			
(City)	(State)	(Zip)												
		Table I	Non-Derivativ	e Securities	Acquire	l, Disp	osed of, or Ben	eficially O	wned					
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial		
			(Wonth/Day/Tear)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (111501.4)	Ownership (Instr.		
Common Stock			04/03/2019		М		6,834	A	\$2.9	2,573,308	D			
Common Stock			04/03/2019		S ⁽¹⁾		18,200	D	\$54.63 ⁽²⁾	2,555,108	D			
Common Stock			04/03/2019		S ⁽¹⁾		200	D	\$55.24(3)	2,554,908	D			
Common Stock			04/03/2019		S ⁽¹⁾		1,418	D	\$54.6 ⁽⁴⁾	71,180	I	By Family Partnership		
Common Stock			04/04/2019		M		6,834	A	\$2.9	2,561,742	D			
Common Stock			04/04/2019		S ⁽¹⁾		13,900	D	\$53.17 ⁽⁵⁾	2,547,842	D			
Common Stock			04/04/2019		S ⁽¹⁾		2,700	D	\$54.24 ⁽⁶⁾	2,545,142	D			
Common Stock			04/04/2019		S ⁽¹⁾		1,800	D	\$55.14 ⁽⁷⁾	2,543,342	D			
Common Stock			04/04/2019		S ⁽¹⁾		1,118	D	\$53.12 ⁽⁸⁾	70,062	I	By Family Partnership		
Common Stock			04/04/2019		S ⁽¹⁾		200	D	\$53.97(9)	69,862	I	By Family Partnership		
Common Stock			04/04/2019		S ⁽¹⁾		100	D	\$55.13	69,762	I	By Family Partnership		
Common Stock										20,000	I	By Spouse		

			Т	able I -	Non-Deri	ative Se	curities A	Acquired,	Dispose	ed of, or	r Beneficially Ov	vned								
1. Title of Security (Instr. 3)					Date	Date Execution Date, 0		3. Transaction Code (Instr.		Securities a str. 3, 4 and	Acquired (A) or Dispos	` ′ В	Amount of Securit	Dir	Ownership Form: rect (D) or Indirect	7. Nature of Indirect Beneficial				
					(Month/Day/		41- /D O4 1	Code	V Amo	ount	(A) or (D)		ollowing Reported ransaction(s) (Instr.		(Instr. 4)	Beneficial Ownership (Instr. 4)				
Common Stock													60,946 I							
Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)																				
1. Title of Derivative Security (Instr. 3)	or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)		Securities A	of Derivative Acquired (A) of of (D) (Instr. 3	or Expiration			Title and Amount of Serivative Security (Instr		Derivative Security (Instr. 5) deriv		Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Inst				
Derivative Security Derivative Security Date Expiration Number of Transaction(s) Code V (A) (D) Exercisable Date Title Shares (Instr. 4)													4)							
Stock Option (Right to Buy)	\$2.9	04/03/2019		М			6,834	(11)	06/09/	/2020	Common Stock	6,834	\$0.00	307,548	B D					
Stock Option (Right to Buy)	\$2.9	04/04/2019		M			6,834	(11)	06/09/	/2020	Common Stock	6,834	\$0.00	300,714	l D					

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$54.20 to \$55.17. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$55.22 to \$55.26. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$54.29 to \$55.12. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$52.79 to \$53.74. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$53.80 to \$54.78. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$54.88 to \$55.46. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$52.77 to \$53.57. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$53.80 to \$54.17. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 11. Fully vested.

Remarks:

/s/ Michael Lowenstein, Attorney-in-fact

04/05/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
l	Estimated average burden	
١	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person			N INC FGEN		OI .				tionship of Reporting Person(s) all applicable) Director	to Issuer	ner				
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 04/17/2019	est Transaction (M	lonth/Day/Y	ear)			X	Officer (give title below)		pecify below)				
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	al Filed (Mo	nth/Day	/Year)			Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person						
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person					
(City)	(State)	(Zip)														
		Table I	- Non-Derivativ	ve Securities /	Acquired	d, Disp	oosed of, or Ben	wned								
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	3. Transac Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial					
			(Month Day Tear)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (111811. 4)	Ownership (Instr. 4)				
Common Stock			04/17/2019		М		6,834	A	\$2.9	2,550,176	D					
Common Stock			04/17/2019		S ⁽¹⁾		14,836	D	\$46.6 ⁽²⁾	2,535,340	D					
Common Stock			04/17/2019		S ⁽¹⁾		3,464	D	\$47.17(3)	2,531,876	D					
Common Stock			04/17/2019		S ⁽¹⁾		100	D	\$48.75	2,531,776	D					
Common Stock			04/17/2019		S ⁽¹⁾		1,318	D	\$46.6(4)	68,444	I	By Family Partnership				
Common Stock			04/17/2019		S ⁽¹⁾		100	D	\$47.09	68,344	I	By Family Partnership				
Common Stock			04/18/2019		М		6,834	A	\$2.9	2,538,610	D					
Common Stock		04/18/2019		S ⁽¹⁾		3,217	D	\$45.69(5)	2,535,393	D						
Common Stock			04/18/2019		S ⁽¹⁾		8,625	D	\$46.82(6)	2,526,768	D					
Common Stock			04/18/2019		S ⁽¹⁾		6,558	D	\$47.34 ⁽⁷⁾	2,520,210	D					
Common Stock			04/18/2019		S ⁽¹⁾		200	D	\$45.33 ⁽⁸⁾	68,144	I	By Family Partnership				
Common Stock			04/18/2019		S ⁽¹⁾		1,218	D	\$47.13 ⁽⁹⁾	66,926	I	By Family Partnership				
1				1			1	1		1	1					

			Т	able I -	Non-Deriv	ative Sec	urities A	cquired, I	Disposed	l of, or Be	neficially O	wned				
1. Title of Security (Instr. 3)					2. Transactio	Executi		3. Transactio Code (Instr. 8		curities Acqu r. 3, 4 and 5)	ired (A) or Dispo		5. Amount of Securiti	Dire	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial
					(Month/Day/Y	ear) if any (Month/	/Day/Year)	Code V	Amo	unt	(A) or (D)		Following Reported Transaction(s) (Instr. 4)		Instr. 4)	Ownership (Inst
Common Stock													20,000		I	By Spouse
Common Stock													60,946		I	See footnote ⁽¹⁰⁾
	T.	l	l		(e.g., p	uts, calls,	warrant	s, options	, conver	tible secu			l	I		I
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)		5. Number of Securities Aco Disposed of (4 and 5)	quired (A) o	r Expiration			and Amount of S ve Security (Insti	ecurities Underlyii r. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	Form: Direct (D) or Indirect	Indirect Beneficial Ownership (Ins
	Derivative Security			Code	v	(A)	(D)	Date Exercisab	Expirat le Date	ion Title		Amount or Number of Shares		Owned Following Reported Transaction((Instr. 4)	s)	4)
Stock Option (Right to Buy)	\$2.9	04/17/2019		М			6,834	(11)	06/09/2	020 Co	ommon Stock	6,834	\$0.00	293,880	D	
Stock Option (Right to Buy)	\$2.9	04/18/2019		М			6,834	(11)	06/09/2	020 C	ommon Stock	6,834	\$0.00	287,046	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$46.01 to \$46.99. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$47.00 to \$47.71. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$46.07 to \$46.8775. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$45.18 to \$46.16. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$46.19 to \$47.185. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$47.19 to \$47.54. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$45.03 to \$45.63. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$46.535 to \$47.40. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.

11. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

04/19/2019 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROV	AL
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re	eporting Person*			and Ticker or Trac VINC [FGEN		ol			tionship of Reporting Person(s all applicable) Director) to Issuer 10% Ov	/por				
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 05/13/2019	est Transaction (M	onth/Day/Y	ear)			X	Officer (give title below)		pecify below)			
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		I .	Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person					
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person				
(City)	(State)	(Zip)	-												
		Table I	- Non-Derivativ	e Securities /	Acquired	d, Disp	osed of, or Ben	eficially O	wned						
1. Title of Security (Instr. 3))		2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transac Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial			
			((Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (11)	Ownership (Instr.			
Common Stock			05/13/2019		М		6,834	A	\$2.9	2,527,044	D				
Common Stock			05/13/2019		S ⁽¹⁾		6,200	D	\$35.23(2)	2,520,844	D				
Common Stock			05/13/2019		S ⁽¹⁾		11,500	D	\$36.07(3)	2,509,344	D				
Common Stock			05/13/2019		S ⁽¹⁾		700	D	\$36.92(4)	2,508,644	D				
Common Stock			05/13/2019		S ⁽¹⁾		918	D	\$35.52(5)	66,008	I	By Family Partnership			
Common Stock			05/13/2019		S ⁽¹⁾		500	D	\$36.21(6)	65,508	I	By Family Partnership			
Common Stock			05/14/2019		М		6,834	A	\$2.9	2,515,478	D				
Common Stock			05/14/2019		S ⁽¹⁾		6,350	D	\$36.4(7)	2,509,128	D				
Common Stock			05/14/2019		S ⁽¹⁾		12,050	D	\$37.12(8)	2,497,078	D				
Common Stock			05/14/2019		S ⁽¹⁾		1,100	D	\$36.77(9)	64,408	I	By Family Partnership			
Common Stock			05/14/2019		S ⁽¹⁾		318	D	\$37.37(10)	64,090	I	By Family Partnership			
Common Stock										20,000	I	By Spouse			

			Т	able I -	Non-Deriv	ative Se	curities A	Acquired,	Dispose	ed of,	or Beneficially Ov	/ned				
1. Title of Security (Instr. 3)					2. Transaction 2A. Deemed Execution E (Month/Day/Year) if any		ution Date,	3. Transacti Code (Instr.		Securitionstr. 3, 4	es Acquired (A) or Dispos and 5)	`´ B	. Amount of Securit seneficially Owned	Dir	Ownership Form: rect (D) or Indirect	7. Nature of Indirect Beneficial
					(Month/Day/	(Mont	th/Day/Year)	Code	V Am	mount	(A) or (D)		ollowing Reported ransaction(s) (Instr.)		(Instr. 4)	Ownership (Insti
Common Stock													60,946		I	See footnote ⁽¹¹⁾
				Table I				•	•	•	r Beneficially Own securities)	ed				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)		Securities A	of Derivative Acquired (A) of f (D) (Instr. 3	or Expiration	Exercisable on Date Day/Year)		7. Title and Amount of Se Derivative Security (Instr.		Derivative deriva Security (Instr. Securi 5) Benefi		Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Ins
	Derivative Security			Code	v	(A)	(D)	Date Exercisa		iration	Title	Amount or Number of Shares		Owned Following Reported Transaction (Instr. 4)	n(s)	4)
Stock Option (Right to Buy)	\$2.9	05/13/2019		M			6,834	(12)	06/09	9/2020	Common Stock	6,834	\$0.00	280,212	D	
Stock Option (Right to Buy)	\$2.9	05/14/2019		M			6,834	(12)	06/09	9/2020	Common Stock	6,834	\$0.00	273,378	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$34.75 to \$35.74. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price
- 3. The shares were sold at prices ranging from \$35.75 to \$36.67. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$36.82 to \$37.24. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$34.97 to \$35.91. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$36.00 to \$36.41. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$35.77 to \$36.76. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$36.77 to \$37.64. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$36.23 to \$37.305. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 10. The shares were sold at prices ranging from \$37.32 to \$37.43. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 11. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 12. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

** Signature of Reporting Person

05/15/2019 Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

^{*} If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

^{**} Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep Neff Thomas B	orting Person [*]						icker or Trac		ol					eck all ap	nip of Reporting Poplicable)	erson(s)	to Issuer	10% Owr	er
(Last) C/O FIBROGEN, INC.	(First)	(M	iddle)		3. Date of 05/22/201		ansaction (M	lonth/Day/`	Year)						Officer (give title		cutive O	Other (sp	ecify below)
409 ILLINOIS ST.					4. If Amen	dment, Da	te of Origina	al Filed (Mo	onth/Day	/Year)			6. In		or Joint/Group F Form filed by On	٠,	• • •	,	
(Street) SAN FRANCISCO	CA	94	158												Form filed by Mo	ore than (One Repo	orting Person	
(City)	(State)	(Zi	p)																
			Т	able I - I	Non-Deriv	ative S	ecurities .	Acquire	d, Disp	osed of	f, or Ben	eficially O	wned						
1. Title of Security (Instr. 3)					2. Transaction	Exe	Deemed cution Date,	3. Transa Code (In:		4. Securi		ed (A) or Dispo	sed Of (D)	Ber	Amount of Securiti	es	Direct (E	rship Form: D) or Indirect	7. Nature of Indirect
					(Month/Day/\		y nth/Day/Year)	Code	v	Amount		(A) or (D)	Price		lowing Reported nsaction(s) (Instr.	3 and	(I) (Instr.	. 4)	Beneficial Ownership (Instr. 4)
Common Stock					05/22/20	19		М		6,	,834	A	\$2.9		2,503,912			D	
Common Stock					05/22/20	19		S ⁽¹⁾		18	3,400	D	\$35.73(2	2)	2,485,512			D	
Common Stock					05/22/20	19		S ⁽¹⁾		1,	,418	D	\$35.71(3	()	62,672			I	By Family Partnership
Common Stock					05/23/20	19		M		6,	,834	A	\$2.9		2,492,346			D	
Common Stock					05/23/20	19		S ⁽¹⁾		17	,300	D	\$35(4)		2,475,046			D	
Common Stock					05/23/20	19		S ⁽¹⁾		1,	,100	D	\$35.25(5	9	2,473,946			D	
Common Stock					05/23/20	19		S ⁽¹⁾		1,	,418	D	\$35.05(6	i)	61,254			I	By Family Partnership
Common Stock															20,000			I	By Spouse
Common Stock															60,946			I	See footnote ⁽⁷⁾
				Table I			urities Ac					icially Owi	ned						
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)		Securities	of Derivative Acquired (A) of (D) (Instr.	or Expir	te Exercis ation Dat th/Day/Ye			d Amount of S Security (Inst		Security (Instr. Securities (D) or Indirect Beneficial 5) Beneficially (I) (Instr. 4) Ownership (Instr.			Indirect Beneficial		
	Security				1 1								- 1		1	Followi			l <i>'</i>

			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$2.9	05/22/2019	M			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	266,544	D	
Stock Option (Right to Buy)	\$2.9	05/23/2019	М			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	259,710	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$35.28 to \$36.22. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$35.45 to \$36.03. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$34.23 to \$35.22. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$35.23 to \$35.30. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$34.73 to \$35.18. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

05/24/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROV	AL
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person [*]			and Ticker or Trac		ol				tionship of Reporting Person(s) all applicable) Director	to Issuer	ner
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 06/05/2019	est Transaction (M	onth/Day/Y	ear)			X	Officer (give title below)		pecify below)
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)		6. Indiv	•	rting Person	
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person	
(City)	(State)	(Zip)										
		Table I	- Non-Derivati	ve Securities /	Acquire	d, Disp	osed of, or Ben	eficially O	wned			
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	d (A) or Dispo	sed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect Beneficial
			(Month/Day/Tear)	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Ownership (Instr. 4)
Common Stock			06/05/2019		М		6,834	A	\$2.9	2,480,780	D	
Common Stock			06/05/2019		S ⁽¹⁾		16,878	D	\$38.43(2)	2,463,902	D	
Common Stock			06/05/2019		S ⁽¹⁾		1,522	D	\$38.97(3)	2,462,380	D	
Common Stock			06/05/2019		S ⁽¹⁾		1,418	D	\$38.52(4)	59,836	I	By Family Partnership
Common Stock			06/06/2019		М		6,834	A	\$2.9	2,469,214	D	
Common Stock			06/06/2019		S ⁽¹⁾		6,900	D	\$37.57(5)	2,462,314	D	
Common Stock			06/06/2019		S ⁽¹⁾		11,500	D	\$38.16(6)	2,450,814	D	
Common Stock			06/06/2019		F ⁽⁷⁾		8,542	D	\$38.31	2,442,272	D	
Common Stock			06/06/2019		S ⁽¹⁾		800	D	\$37.77(8)	59,036	I	By Family Partnership
Common Stock			06/06/2019		S ⁽¹⁾		618	D	\$38.2(9)	58,418	I	By Family Partnership
Common Stock										20,000	I	By Spouse
Common Stock										60,946	I	See footnote ⁽¹⁰⁾

				Table II			-			or Beneficially Owne e securities)	ed				
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transad (Instr. 8)	ction Code	5. Number of Securities Ac Disposed of 4 and 5)	quired (A) or	6. Date Exerc Expiration D (Month/Day/Y	ate	7. Title and Amount of Sec Derivative Security (Instr. 3		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.9	06/05/2019		M			6,834	(11)	06/09/2020	Common Stock	6,834	\$0.00	252,876	D	
Stock Option (Right to Buy)	\$2.9	06/06/2019		М			6,834	(11)	06/09/2020	Common Stock	6,834	\$0.00	246,042	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$37.88 to \$38.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$38.885 to \$39.03. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$38.12 to \$39.01. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$36.935 to \$37.93. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$37.945 to \$38.49. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. Represents shares withheld by the issuer to satisfy a tax obligation realized by the reporting person upon the vesting of restricted stock units.
- 8. The shares were sold at prices ranging from \$37.12 to \$38.09. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$38.155 to \$38.25. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 11. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/07/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person [*]					and Ticker or Trad	0 ,	ol				ionship of Reporting Person(s all applicable) Director	s) to Issuer	/ner
(Last) C/O FIBROGEN, INC.	(First)	(Mid	ddle)		Date of Earlie /19/2019	st Transaction (M	onth/Day/Y	ear)			X	Officer (give title below		pecify below)
409 ILLINOIS ST.				4. If	If Amendmer	t, Date of Origina	Filed (Mo	nth/Day/	/Year)		6. Indivi	dual or Joint/Group Filing (C		
(Street) SAN FRANCISCO	CA	941	158									·	n One Reporting Person	
(City)	(State)	(Zip	o)											
			T	able I - Non-	-Derivativ	e Securities A	cquirec	d, Disp	osed of, or Ber	neficially O	wned			
1. Title of Security (Instr. 3)				Date		2A. Deemed Execution Date,	3. Transac Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	red (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect
				(Mon	nth/Day/Year)	if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)
Common Stock				06.	5/19/2019		M		6,834	A	\$2.9	2,449,106	D	
Common Stock				06.	5/19/2019		S ⁽¹⁾		18,400	D	\$44.02(2)	2,430,706	D	
Common Stock				06.	5/19/2019		S ⁽¹⁾		1,418	D	\$43.99(3)	57,000	I	By Family Partnership
Common Stock				06.	5/20/2019		M		6,834	A	\$2.9	2,437,540	D	
Common Stock				06.	5/20/2019		S ⁽¹⁾		16,200	D	\$44.28(4)	2,421,340	D	
Common Stock				06.	5/20/2019		S ⁽¹⁾		2,200	D	\$45.22(5)	2,419,140	D	
Common Stock				06.	5/20/2019		S ⁽¹⁾		1,318	D	\$44.23(6)	55,682	I	By Family Partnership
Common Stock				06.	5/20/2019		S ⁽¹⁾		100	D	\$45.45	55,582	I	By Family Partnership
Common Stock												20,000	I	By Spouse
Common Stock												60,946	I	See footnote ⁽⁷⁾
									sed of, or Bene nvertible secur		ned			
Title of Derivative Security (Instr. 3)	Conversion	3. Transaction n Date e (Month/Day/Year)	3A. Deemed Execution Date, if any	4. Transaction (Instr. 8)	Code 5. Nu Secu	mber of Derivative rities Acquired (A) o osed of (D) (Instr. 3	6. Date	Exercis	sable and 7. Title a		Securities Underly tr. 3 and 4)	8. Price of Derivative Security (Instr. Security		Indirect

I		Price of		(Month/Day/Year)			4 and 5)						5)		(I) (Instr. 4)	Ownership (Instr.
		Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		(4)
Stock Option (Right to Bu	uy)	\$2.9	06/19/2019		M			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	239,208	D	
Stock Option (Right to Bu	uy)	\$2.9	06/20/2019		M			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	232,374	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$43.60 to \$44.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$43.695 to \$44.59. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$43.92 to \$44.865. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$44.92 to \$45.48. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.

 6. The shares were sold at prices ranging from \$44.02 to \$44.85. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

06/21/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	porting Person [*]				FIBROGI	e and Ticker or Trac EN INC [FGEN]					tionship of Reporting Pers all applicable) Director	on(s) to Issue	10% Owr	ner
(Last) C/O FIBROGEN, INC.	(First)	(N	Middle)		3. Date of Ea 07/10/2019	rliest Transaction (M	lonth/Day/\	'ear)			X		elow) of Executive (٠.	pecify below)
409 ILLINOIS ST.					4. If Amendm	ent, Date of Origina	al Filed (Mo	onth/Day	/Year)		6. Indiv	idual or Joint/Group Filin Form filed by One I		,	
(Street) SAN FRANCISCO	CA	92	4158									Form filed by More	than One Rep	oorting Person	
(City)	(State)	(Z	ip)												
			Т	able I - N	Non-Deriva	ive Securities	Acquire	d, Disp	oosed of, or E	Beneficially C)wned				
1. Title of Security (Instr. 3)					2. Transaction Date (Month/Day/Yea	2A. Deemed Execution Date, r) if any	3. Transa Code (Ins		4. Securities Acc (Instr. 3, 4 and 5	quired (A) or Disp	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported		ership Form: D) or Indirect	7. Nature of Indirect Beneficial
					(мопильаултеа	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 a		r. 4)	Ownership (Instr.
Common Stock					07/10/2019		М		6,834	A	\$2.9	2,425,974		D	
Common Stock					07/10/2019		S ⁽¹⁾		12,167	D	\$44.66(2)	2,413,807		D	
Common Stock					07/10/2019		S ⁽¹⁾		6,233	D	\$45.07(3)	2,407,574		D	
Common Stock					07/10/2019		S ⁽¹⁾		1,418	D	\$44.81(4)	54,164		I	By Family Partnership
Common Stock					07/11/2019		М		6,834	A	\$2.9	2,414,408		D	
Common Stock					07/11/2019		S ⁽¹⁾		17,900	D	\$45.14 ⁽⁵⁾	2,396,508		D	
Common Stock					07/11/2019		S ⁽¹⁾		500	D	\$45.66(6)	2,396,008		D	
Common Stock					07/11/2019		S ⁽¹⁾		1,418	D	\$45.09 ⁽⁷⁾	52,746		I	By Family Partnership
Common Stock												20,000		I	By Spouse
Common Stock												60,946		I	See footnote ⁽⁸⁾
				Table II		e Securities Ac s, calls, warran					ned				
Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of		3A. Deemed Execution Date, if any (Month/Day/Year)	(Instr. 8)	ction Code 5. Se	Number of Derivative curities Acquired (A) sposed of (D) (Instr. and 5)	6. Dat	-	sable and 7. Titl	e and Amount of a		Derivative d Security (Instr. S	. Number of erivative ecurities eneficially	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	Indirect

	Derivative Security		Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.9	07/10/2019	M			6,834	(9)	06/09/2020	Common Stock	6,834	\$0.00	225,540	D	
Stock Option (Right to Buy)	\$2.9	07/11/2019	M			6,834	(9)	06/09/2020	Common Stock	6,834	\$0.00	218,706	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$44.035 to \$44.99. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$45.00 to \$45.20. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$44.23 to \$45.13. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$44.56 to \$45.52. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$45.60 to \$45.69. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$44.55 to \$45.34. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 9. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/12/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep	porting Person*		I .	and Ticker or Trac	0 ,	ol				tionship of Reporting Person(s all applicable) Director	t) to Issuer			
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earli 07/24/2019	est Transaction (M	onth/Day/Y	ear)		X	Officer (give title below)		pecify below)			
409 ILLINOIS ST.			4. If Amendme	nt, Date of Origina	l Filed (Mo	nth/Day	/Year)	- 1	Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person					
(Street) SAN FRANCISCO	CA	94158							Form filed by More than	One Reporting Person				
(City)	(State)	(Zip)												
		Tab	ole I - Non-Derivativ	e Securities	Acquired	d, Disp	oosed of, or Ber	neficially O	wned					
1. Title of Security (Instr. 3)			2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any	3. Transac Code (Ins		4. Securities Acquir (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned Following Reported	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial		
			(monta/bay/real/	(Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Transaction(s) (Instr. 3 and 4)	(1) (111541.4)	Ownership (Instr.		
Common Stock			07/24/2019		М		6,834	A	\$2.9	2,402,842	D			
Common Stock			07/24/2019		S ⁽¹⁾		18,400	D	\$46.54(2)	2,384,442	D			
Common Stock			07/24/2019		S ⁽¹⁾		1,418	D	\$46.57 ⁽³⁾	51,328	I	By Family Partnership		
Common Stock			07/25/2019		М		6,834	A	\$2.9	2,391,276	D			
Common Stock			07/25/2019		S ⁽¹⁾		16,500	D	\$46.86(4)	2,374,776	D			
Common Stock			07/25/2019		S ⁽¹⁾		1,900	D	\$47.72(5)	2,372,876	D			
Common Stock			07/25/2019		S ⁽¹⁾		1,318	D	\$46.8(6)	50,010	I	By Family Partnership		
Common Stock			07/25/2019		S ⁽¹⁾		100	D	\$47.9	49,910	I	By Family Partnership		
Common Stock										20,000	I	By Spouse		
Common Stock										60,946	I	See footnote ⁽⁷⁾		
		Т	able II - Derivative (e.g., puts				sed of, or Bene onvertible secur		ned					
Title of Derivative Security (Instr. 3)	Conversion		nstr. 8) Secu	mber of Derivative rities Acquired (A) osed of (D) (Instr. 3	or Expira	tion Dat	te Derivativ	nd Amount of S e Security (Ins	Securities Underl tr. 3 and 4)	ying 8. Price of 9. Nui Derivative deriva Security (Instr. Secur	tive Form: Direct	11. Nature of Indirect Beneficial		

1	Price of		(Month/Day/Year)			4 and 5)						5)		(I) (Instr. 4)	Ownership (Instr.
	Derivative Security			Code	v	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares		Owned Following Reported Transaction(s) (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.9	07/24/2019		M			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	211,872	D	
Stock Option (Right to Buy)	\$2.9	07/25/2019		M			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	205,038	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$46.20 to \$47.01. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$46.28 to \$46.97. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$46.27 to \$47.22. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$47.28 to \$47.96. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price. 6. The shares were sold at prices ranging from \$46.34 to \$47.08. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

07/26/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

	OMB APPROVAL	
	OMB Number:	3235-0287
ı	Estimated average burden	
ı	hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(h)

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Re Neff Thomas B	eporting Person [*]			e and Ticker or Trace N INC [FGEN		ol		(Che	lationship of Reporting Person(s ck all applicable) X Director) to Issuer	uner.			
(Last) C/O FIBROGEN, INC.	(First)	(Middle)	3. Date of Earl 08/12/2019	iest Transaction (M	lonth/Day/\	ear)				X Officer (give title below) Other (specify below) Chief Executive Officer				
409 ILLINOIS ST.			4. If Amendme	ent, Date of Origina	al Filed (Mo	nth/Day	/Year)		lividual or Joint/Group Filing (C					
(Street) SAN FRANCISCO	CA	94158								Form filed by More than	One Reporting Person			
(City)	(State)	(Zip)												
		Table	I - Non-Derivati	ve Securities	Acquire	d, Disp	posed of, or Ben	eficially O	wned					
1. Title of Security (Instr. 3))		2. Transaction Date	2A. Deemed Execution Date,	3. Transa Code (Ins		4. Securities Acquire (Instr. 3, 4 and 5)	ed (A) or Dispo	osed Of (D)	5. Amount of Securities Beneficially Owned	6. Ownership Form: Direct (D) or Indirect	7. Nature of Indirect		
			(Month/Day/Year)) if any (Month/Day/Year)	Code	v	Amount	(A) or (D)	Price	Following Reported Transaction(s) (Instr. 3 and 4)	(I) (Instr. 4)	Beneficial Ownership (Instr. 4)		
Common Stock			08/12/2019		М		6,834	A	\$2.9	2,379,710	D			
Common Stock			08/12/2019		S ⁽¹⁾		10,700	D	\$44.98(2)	2,369,010	D			
Common Stock			08/12/2019		S ⁽¹⁾		7,700	D	\$45.59 ⁽³⁾	2,361,310	D			
Common Stock			08/12/2019		S ⁽¹⁾		1,118	D	\$45.04(4)	48,792	I	By Family Partnership		
Common Stock			08/12/2019		S ⁽¹⁾		300	D	\$45.67(5)	48,492	I	By Family Partnership		
Common Stock			08/13/2019		М		6,834	A	\$2.9	2,368,144	D			
Common Stock			08/13/2019		S ⁽¹⁾		11,500	D	\$45.33(6)	2,356,644	D			
Common Stock			08/13/2019		S ⁽¹⁾		6,900	D	\$46.19 ⁽⁷⁾	2,349,744	D			
Common Stock			08/13/2019		S ⁽¹⁾		918	D	\$45.31(8)	47,574	I	By Family Partnership		
Common Stock			08/13/2019		S ⁽¹⁾		500	D	\$46.17(9)	47,074	I	By Family Partnership		
Common Stock										20,000	I	By Spouse		
Common Stock										60,946	I	See footnote ⁽¹⁰⁾		

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned																	
1. Title of Security (Instr. 3)			2. Transacti Date	Exe	Execution Date,		tion r. 8)	4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)				5. Amount of Securities Beneficially Owned		Ownership Form: rect (D) or Indirect	7. Nature of Indirect		
		(Month/Day/	(Mo	nth/Day/Year)	Code	v	Amount	(A)	A) or (D)	Price	Following Reported Transaction(s) (Instr. 4)		(Instr. 4)	Beneficial Ownership (Instr. 4)			
	Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)																
1. Title of Derivative Security (Instr. 3)	Price of	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	(Instr. 8) Se		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underly Derivative Security (Instr. 3 and 4)		Derivative de Security (Instr. 5)		Form: Direct (D) or Indirect	11. Nature of Indirect Beneficial Ownership (Instr.	
	Derivative Security			Code	v	(A)	(D)	Date Exercis		Expiration Date	Title		Amount or Number of Shares		Owned Following Reported Transaction (Instr. 4)		4)
Stock Option (Right to Buy)	\$2.9	08/12/2019		M			6,834	(11)) (06/09/2020	Common	n Stock	6,834	\$0.00	198,204	4 D	
Stock Option (Right to Buy)	\$2.9	08/13/2019		M			6,834	(11)) (06/09/2020	Common	n Stock	6,834	\$0.00	191,370) D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$44.42 to \$45.41. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$45.42 to \$45.90. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$44.50 to \$45.46. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$45.515 to \$45.76. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$44.94 to \$45.93. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares were sold at prices ranging from \$45.94 to \$46.60. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 8. The shares were sold at prices ranging from \$44.98 to \$45.82. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 9. The shares were sold at prices ranging from \$46.00 to \$46.37. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 10. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 11. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/14/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden	
hours per response:	0.5

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

1. Name and Address of Rep	orting Person*						Ticker or Tra	0 ,	ol					Relationship of Reporting Person(s) to Issuer (Check all applicable)						
Neff Thomas B							VC [FGEN	3					1,		olicable) Director			10% Owr	er	
(Last) C/O FIBROGEN, INC.	(First)	(M	1iddle)		3. Date of 08/21/201		ransaction (M	lonth/Day/\	rear))	X C	Officer (give title	,	ecutive Of	` '	ecify below)	
409 ILLINOIS ST.					4. If Amer	ndment, D	ate of Origina	al Filed (Mo	onth/Day	/Year)					or Joint/Group F	٠,	• • •	,		
(Street) SAN FRANCISCO	CA	94	1158											F	Form filed by Mo	re than (One Repor	ting Person		
(City)	(State)	(Z	ip)																	
			Т	able I -	Non-Deri	vative S	Securities	Acquire	d, Disp	osed of	f, or Ben	eficially O	wned							
1. Title of Security (Instr. 3)					2. Transacti Date (Month/Day/	Ex	Deemed ecution Date,	3. Transa Code (Ins		4. Securi (Instr. 3,		d (A) or Dispo	sed Of (D)	Bene	nount of Securiti eficially Owned	es	Direct (D)	ship Form: or Indirect	7. Nature of Indirect Beneficial	
					(Month/Day/		onth/Day/Year)	Code	v	Amount		(A) or (D)	Price		saction(s) (Instr.	3 and	(I) (Instr. 4	1)	Ownership (Instr. 4)	
Common Stock					08/21/20	19		М		6,	,834	A	\$2.9		2,356,578			D		
Common Stock					08/21/20	19		S ⁽¹⁾		18	3,400	D	\$44.79 ⁽²⁾		2,338,178			D		
Common Stock					08/21/20	19		S ⁽¹⁾		1,	,418	D	\$44.81 ⁽³⁾		45,656			I	By Family Partnership	
Common Stock					08/22/20	19		М		6,	,834	A	\$2.9		2,345,012			D		
Common Stock					08/22/20	19		S ⁽¹⁾		17	7,100	D	\$43.8(4)		2,327,912			D		
Common Stock					08/22/20	19		S ⁽¹⁾		1.	,300	D	\$44.73 ⁽⁵⁾		2,326,612			D		
Common Stock					08/22/20	19		S ⁽¹⁾		1,	,418	D	\$43.77(6)		44,238			I	By Family Partnership	
Common Stock															20,000			I	By Spouse	
Common Stock	on Stock														60,946			I	See footnote ⁽⁷⁾	
	Table			curities Ad					icially Owi	ned										
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transa (Instr. 8)	ection Code	Securitie	er of Derivative s Acquired (A) l of (D) (Instr.	or Expira	e Exercis ation Dat h/Day/Ye			d Amount of S Security (Inst	ecurities Under r. 3 and 4)		Derivative Security (Instr. 5)		ive Feies (I	0. Ownership orm: Direct D) or Indirect) (Instr. 4)	Indirect	

			Code	v	(A)	(D)	Date Exercisable	Expiration Date		Amount or Number of Shares		Reported Transaction(s) (Instr. 4)		
Stock Option (Right to Buy)	\$2.9	08/21/2019	M			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	184,536	D	
Stock Option (Right to Buy)	\$2.9	08/22/2019	М			6,834	(8)	06/09/2020	Common Stock	6,834	\$0.00	177,702	D	

Explanation of Responses:

- 1. Shares sold pursuant to a 10b5-1 plan.
- 2. The shares were sold at prices ranging from \$44.54 to \$45.12. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 3. The shares were sold at prices ranging from \$44.51 to \$45.115. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 4. The shares were sold at prices ranging from \$43.46 to \$44.38. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 5. The shares were sold at prices ranging from \$44.61 to \$44.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 6. The shares were sold at prices ranging from \$43.47 to \$43.95. The reporting person will provide upon request to the SEC, the issuer or security holder of the issuer, full information regarding the number of shares sold at each separate price.
- 7. The shares are held by BioGrowth Partners, LP. The reporting person is the sole general partner of BioGrowth Partners, LP and has sole voting and dispositive power over the shares held by BioGrowth Partners, LP.
- 8. Fully vested.

Remarks:

/s/ Dorothy Pacini, Attorney-in-fact

08/23/2019

** Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.